UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF NEW YORK

IN RE ALKERMES PUBLIC LIMITED COMPANY SECURITIES LITIGATION

Case No.: 1:18-CV-07410-LDH-SMG

DEMAND FOR JURY TRIAL

CONSOLIDATED CLASS ACTION COMPLAINT FOR VIOLATIONS OF THE FEDERAL SECURITIES LAWS

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GLOSSARY

Term	Explanation
ALKS 5461	An opioid combination product containing buprenorphine and samidorphan, intended to be used in the treatment of Major Depressive Disorder.
Breakthrough Therapy Designation	Breakthrough Therapy Designation is a process designed to expedite the development and review of drugs that are intended to treat a serious condition when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s).
Endpoint	An endpoint in a clinical trial, for instance in a trial evaluating the efficacy of a new medical product, measures the desired clinical outcomes produced in the trial.
Investigational New Drug application ("IND")	An Investigational New Drug application ("IND") is the first step in the drug review process by the U.S. Food and Drug Administration ("FDA"). The application is submitted by the company responsible for developing the drug (the sponsor) to the FDA.
Montgomery-Åsberg Depression Rating Scale ("MADRS")	The Montgomery-Åsberg Depression Rating Scale ("MADRS") is a diagnostic questionnaire used to measure the severity of depressive episodes in patients with mood disorders.
Major Depressive Disorder ("MDD")	Major Depressive Disorder ("MDD") is a mental health disorder characterized by persistently depressed mood or loss of interest in activities, causing significant impairment in daily life.
New Drug Application ("NDA")	The New Drug Application ("NDA") is the formal final step taken by a drug sponsor, which involves applying to the FDA to get the approval required to market a new drug in the U.S.
Refusal-to-file action ("RTF letter")	A refusal-to-file action ("RTF letter") allows the FDA to inform a sponsor as quickly as possible of deficiencies in an NDA. Within 30 days of the date of the review division's RTF notification, the applicant may request an informal conference with

	the FDA to discuss whether the FDA should file the application. If, after the informal conference, the applicant requests that the review division file the application (with or without amendments to correct the deficiencies), the review division will file the application and review it as filed. Alternatively, the applicant may amend the NDA and resubmit it, and the review division will make a separate determination whether the resubmitted NDA may be filed.
Sequential Parallel Comparison Design ("SPCD")	Sequential parallel comparison design ("SPCD") is used for trials with high placebo response. In the first stage of SPCD subjects are randomized between placebo and active treatment. In the second stage placebo non-responders are re-randomized between placebo and active treatment. Data from the population of "all comers" and the subpopulations of placebo non-responders are then combined to yield a single p-value for treatment comparison.
Statistical Analysis Plan ("SAP")	A statistical analysis plan ("SAP") defines guidelines for the analysis and presentation of data at various stages of a trial.

Lead Plaintiff Midwest Operating Engineers Pension Trust Fund ("Midwest Operating Engineers" or "Lead Plaintiff"), individually and on behalf of all other persons similarly situated, by their undersigned attorneys, make the following allegations against Alkermes Public Limited Company ("Alkermes" or the "Company"); Richard F. Pops ("Pops"), the Company's Chairman and Chief Executive Officer ("CEO"); James M. Frates ("Frates"), the Company's Senior Vice President and Chief Financial Offer ("CFO"); Elliot Ehrich ("Ehrich"), the Company's Chief Medical Officer ("CMO") and Executive Vice President of Research and Development; and Blair C. Jackson ("Jackson"), Senior Vice President of Corporate Planning (Pops, Frates, Ehrich, and Jackson are the "Individual Defendants," and, together with Alkermes, "Defendants"), based on its personal knowledge, on information and belief, and on the investigation conducted by its counsel. The investigation included, among other things, a review of: United States Securities and Exchange Commission ("SEC") filings by Alkermes; regulatory filings and reports; securities analysts' reports and advisories about Alkermes; transcripts of Alkermes' earnings and other investor conference calls and related presentations; press releases and other public statements issued by Alkermes; media reports about Alkermes; court records; other publicly available information; and consultations with experts. Lead Plaintiff believes that substantial additional evidentiary support will exist for the allegations set forth herein after a reasonable opportunity for discovery.

I. NATURE OF THE ACTION

1. This is a federal securities class action on behalf of all persons other than Defendants and their affiliates who purchased or acquired Alkermes common stock during the period from July 31, 2014 through and including November 1, 2018 (the "Class Period"), which seeks to recover damages caused by Defendants' violations of the Securities Exchange Act of 1934 ("Exchange Act"). Defendants made a series of materially false and misleading statements and

omissions during the Class Period which artificially inflated the price of Alkermes common stock. Later disclosures caused the price of Alkermes common stock to decline, causing injury to Lead Plaintiff and the Class.

2. Alkermes is a global biopharmaceutical company possessing more than 20 commercial drugs. This action arises from material misrepresentations and omissions by Alkermes and the Individual Defendants concerning the viability of ALKS 5461, an opioid combination product developed by Alkermes containing buprenorphine and samidorphan and intended to be used to treat Major Depressive Disorder ("MDD"). If approved, ALKS 5461 would have been the first drug in an entirely new class of drugs to treat MDD.

3. Unbeknownst to investors, the United States Food and Drug Administration ("FDA") had repeatedly conveyed to Alkermes, beginning prior to the Class Period and continuing throughout, and both at in-person meetings and through written correspondence, that the FDA had major concerns regarding Alkermes' clinical development program for ALKS 5461. Significantly, the FDA conveyed to Alkermes on multiple occasions that (i) the FDA objected to Alkermes' use of Sequential Parallel Comparison Design ("SPCD") in its clinical trials; (ii) the FDA did not endorse Alkermes' strategy of comparing dose groups based on averaged measurements over several weeks; (iii) the FDA did not endorse Alkermes' use of MADRS-6 as a primary endpoint, as opposed to MADRS-10, because MADRS-6 omitted four key concepts relevant and important to MDD: "reduced sleep," "reduced appetite," "concentration difficulties," and "suicidal thoughts"; and (iv) the FDA did not believe that the statistical analysis plan ("SAP") used by Alkermes was sufficient to prove efficacy—an essential element that must be proven in order to obtain approval for a new drug.

4. Despite receiving repeated criticism from the FDA regarding these fundamental

aspects of its clinical development program, Defendants failed to inform the Company's investors of any of the FDA's criticisms. Instead, they made numerous public statements throughout the Class Period touting the positive results of the ALKS 5461 clinical development program, characterizing their meetings with the FDA as positive, and leading investors to believe that the FDA's approval of ALKS 5461 was imminent.

5. Defendants' Class Period statements were materially false and misleading when made because they failed to disclose the FDA's criticisms of the clinical development program for ALKS 5461, which contradicted the Company's repeated positive assertions that, among other things: the Company was using methodologies presumably approved by the FDA in its ALKS 5461 clinical development programs; ALKS 5461 had "demonstrated safety, tolerability and efficacy" in its clinical programs; SPCD, a trial design method the Company was using in its Phase 2 and 3 studies for ALKS 5461, was a "state-of-the-art design methodology"; and outcomes of the meetings with the FDA were favorable and indicated that the drug would be approved.

6. The concealed facts were revealed to the public in a series of corrective disclosures in January 2016, April 2018, October 2018, and November 2018.

7. Specifically, on January 21, 2016, Alkermes announced that two of its three Phase 3 efficacy studies failed to meet their prespecified primary efficacy endpoints, but that the studies achieved "statistical significance" through "*post hoc* analyses." Analysts reacted negatively to the disclosure of the results of the Phase 3 efficacy studies; J.P. Morgan, in an analyst report titled "Depressing Outcome for '5461; Still See Meaningful LT Value in ALKS But Stepping to Sidelines For Now" noted that "FORWARD-4 showed a clear trend towards benefit but ended up being a near miss that, ***according to management, would have hit if using different statistical methods***" (emphasis added). The market reacted sharply to this partial corrective disclosure that

the Phase 3 efficacy studies failed to meet their prespecified primary efficacy endpoints under FDA-approved protocols, and that efficacy was being demonstrated through *post hoc* analysis: the Company's stock price dropped ***44.24%*** from a closing price of $60.42 on January 20, 2016, to close at $33.69 on January 21, 2016, on volume of 12,467,289 shares, more than ***five times*** Alkermes' average volume during the month of January.

8. Industry analysts interpreted the reference to "*post hoc* analysis"—the means by which Alkermes claimed to have reached "statistical significance" despite the failure to meet primary efficacy endpoints—to refer to Alkermes' use of SPCD, which Alkermes had disclosed at least by late 2013 as one of the methods to be used in its Phase 2 and 3 efficacy studies. However, the investing public was yet unaware that the FDA had, on multiple occasions, and as early as late 2013, expressed significant concerns to the Company regarding (and had specifically not authorized) the use of SPCD in the ALKS 5461 trials. The full truth regarding the deficiencies of Alkermes' clinical development program for ALKS 5461 was not revealed at that time, however, as Defendants continued to hide the FDA's skepticism and concerns regarding Alkermes' use of SPCD in its studies from the general public for nearly two more years. As a result, Alkermes common stock continued to trade at artificially inflated prices.

9. In fact, over the next couple of years the FDA continued to convey significant concerns surrounding multiple aspects of the ALKS 5461 clinical development program—all of which were hidden from the investing public. For instance, in February 2017, the FDA told Alkermes that it did not endorse using MADRS-6 as a primary efficacy endpoint instead of MADRS-10, and also did not approve of comparing dose groups based on averaged measurements over several weeks. In March 2017, the FDA denied Alkermes' Breakthrough Therapy Designation, noting that it had not determined that MADRS-6 was an acceptable endpoint. In July

2017, the FDA reiterated that MADRS-6 could not be used instead of MADRS-10 because it excluded four key concepts for evaluating MDD: reduced sleep, reduced appetite, concentration difficulties, and suicidal thoughts.

10. Defendants never disclosed the substance of the FDA's concerns and criticisms, and even denied knowledge of any concerns. On April 2, 2018, Alkermes announced that it had received a refusal-to-file ("RTF") letter from the FDA regarding its New Drug Application ("NDA") for ALKS 5461. In discussing the RTF letter, Alkermes feigned surprise, stating that "while we expected there to be questions during the review process, ***in none of these interactions did FDA raise concerns, which would have let*** [sic] ***us to expect an RTF***"(emphasis added), notwithstanding that the FDA had conveyed repeated concerns and criticisms of the ALKS 5461 clinical development program to Alkermes on multiple occasions since at least late-2013. As the significance of Alkermes' partial corrective disclosure was absorbed by the market, the Company's stock price dropped ***22%*** from a closing price of $57.96 on March 29, 2018, to close at $45.23 on April 2, 2018, on volume of 8,053,845 shares, approximately ***ten times*** Alkermes' average volume during the prior month of March.

11. The FDA's significant concerns regarding multiple aspects of the ALKS 5461 clinical development program were finally made public by the FDA itself in stages, on October 30, 2018 and November 1, 2018. On October 30, 2018, the FDA published a briefing document on ALKS 5461 in anticipation of the November 1, 2018 meeting of the Psychopharmacologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee, appointed by the FDA to review Alkermes' NDA for ALKS 5461 (the "Advisory Committees") to discuss and vote on the ALKS 5461 NDA. The briefing document itemized and revealed the multiple occasions on which it had conveyed its significant concerns regarding, and had explicitly

not authorized, key portions of the ALKS 5461 clinical development program. In response, the price of Alkermes common stock marked a single-day decline of 1.4%. On November 1, 2018, the Advisory Committees held their public meeting, presented their concerns, discussed the drug, and ultimately voted 21 to 2 against the approval of ALKS 5461. In response, the price of Alkermes common stock plummeted 7.57%, reflecting a loss of $480 million in market capitalization.

12. The market was shocked by these disclosures. Following the November 1 meeting, numerous analysts expressed surprise at the information that had been withheld by Alkermes, and which the FDA had revealed, writing: "Extent of Differences Between FDA and Company Surprising: . . . It was surprising to us today to hear the amount of disagreement the FDA has on fundamental issues related to the ALKS 5461 program such as how the studies should have been designed and how many of the trials were actually positive and supportive of approval. We are also somewhat surprised by the relative optimism the Alkermes team still maintained for ALKS 5461 despite what were clearly significant objections that must have been voiced by the FDA during the development and review process" (Credit Suisse); "[W]hat did catch my attention was the FDA rebuke on how company didn't appear to heed to [*sic*] FDA advice on trial design and endpoints" (Evercore ISI); "For many committee members, the last minute change and disregard for FDA's guidance was concerning, especially given that MADRS-6 excludes many important categories important in evaluating depression such as lack of sleep, appetite, and suicidal ideation" (Jefferies).

13. As Defendants' prior misrepresentations, omissions, and fraudulent conduct emerged through a series of partial corrective disclosures and became apparent to the market, the price of Alkermes' common stock declined significantly as the prior artificial inflation dissipated. Lead Plaintiff hereby brings claims against each of the Defendants named in this action for the

resulting losses.

II. JURISDICTION AND VENUE

14. The claims asserted herein arise under and pursuant to Sections 10(b) and 20(a) of the Exchange Act, 15 U.S.C. §§ 78j(b) and 78t(a), and the rules and regulations promulgated thereunder, including SEC Rule 10b-5, 17 C.F.R. § 240.10b-5.

15. This Court has jurisdiction over the subject matter of this action pursuant to 28 U.S.C. § 1331 and Section 27 of the Exchange Act.

16. Venue is proper in this District pursuant to Section 27 of the Exchange Act (15 U.S.C. § 78aa) and 28 U.S.C. § 1391(b) and (c) as the Company conducts business within this District, had agents in this District, and/or transacted or is licensed to transact business in this District.

17. In connection with the acts and conduct alleged herein, Defendants, directly or indirectly, used the means and instrumentalities of interstate commerce, including, but not limited to, the mails, interstate telephone communications, the Internet, and the facilities of the national securities markets.

III. PARTIES

18. Lead Plaintiff **Midwest Operating Engineers** is a Taft-Hartley, multiemployer pension fund with over $4.2 billion in assets. During the Class Period, Lead Plaintiff suffered significant losses from its purchases of Alkermes common stock as a result of Defendants' misrepresentations and omissions. Lead Plaintiff's transactions in Alkermes common stock are reflected in the attached certification and Schedule A.

19. Defendant **Alkermes** is a global biopharmaceutical company headquartered in Dublin, Ireland. Alkermes applies its scientific expertise and proprietary technologies to research, develop, and commercialize pharmaceutical products that are designed to address unmet medical

needs of patients in major therapeutic areas. Alkermes has a research and development facility and corporate offices in Waltham, Massachusetts; a research, development, and manufacturing facility in Athlone, Ireland; and a manufacturing facility in Wilmington, Ohio. Shares of Alkermes common stock trade on the NASDAQ stock exchange under the ticker "ALKS."

20. Defendant **Pops** is, and was at all relevant times, Alkermes' CEO and Chairman of the Board of Directors. As Chairman and CEO of the Company, Pops signed all of the Company's Forms 10-K and 10-Q during the Class Period and made statements in press releases, on earnings calls with analysts, and at conferences with analysts.

21. Defendant **Frates** was at all relevant times Alkermes' CFO. As CFO of the Company, Frates signed all of the Company's Forms 10-K and 10-Q during the Class Period and made statements in press releases, on earnings calls with analysts, and at conferences with analysts.

22. Defendant **Ehrich** was Alkermes' CMO and Executive Vice President of Research and Development from September 2011 to May 2017, and Alkermes' Executive Vice President, Research and Development from May 2017 until January 2018. As CMO of the Company, Ehrich attended meetings with the FDA and made statements at conferences with analysts and industry conferences.

23. Defendant **Jackson** is, and was at all relevant times, Alkermes' Senior Vice President of Corporate Planning, and made statements at conferences with analysts.

24. Because of the Individual Defendants' respective positions at the Company, they had access to adverse undisclosed information about the Company's business, operations, finances, and present and future business prospects via access to internal corporate documents; conversations and connections with other corporate officers and employees; attendance at management, sales and/or Board of Directors meetings and committees thereof; and via reports

and other information provided to them in connection therewith. Because of their possession of such information, the Individual Defendants knew or recklessly disregarded that the adverse facts specified herein had not been disclosed to, and were being concealed from, the investing public.

25. The Individual Defendants are liable as direct participants in the wrongs complained of herein. In addition, the Individual Defendants, by reason of their status as senior executive officers, were "controlling persons" within the meaning of Section 20(a) of the Exchange Act and had the power and influence to cause the Company to engage in the unlawful conduct complained of herein. Because of their positions of control, the Individual Defendants were able to and did, directly or indirectly, control the conduct of Alkermes' business.

26. As senior executive officers and/or directors, and as controlling persons of a publicly traded company whose common stock was registered with the SEC pursuant to the Exchange Act, and was traded on the NASDAQ and governed by the federal securities laws, the Individual Defendants had a duty to promptly disseminate accurate and truthful information with respect to Alkermes' financial condition and performance, growth, operations, business, products, markets, management, earnings and present and future business prospects, and to correct any previously issued statements that had become materially misleading or untrue, so that the market price of Alkermes common stock would be based upon truthful and accurate information. The Individual Defendants' misrepresentations and omissions during the Class Period violated these specific requirements and obligations.

27. The Individual Defendants, because of their positions of control and authority as officers and/or directors of the Company, were able to and did control the content of the various SEC filings, press releases, presentations to securities analysts and through them to the investing public, and other public statements pertaining to the Company during the Class Period. Individual

Defendants Pops and Frates would have each been provided with copies of the documents alleged herein to be misleading, including the Company's quarterly and annual filings and the prepared remarks for each of the Company's quarterly earnings conference calls, prior to or shortly after their issuance and had the ability or opportunity to prevent their issuance or cause them to be corrected. All Individual Defendants made remarks regarding ALKS 5461 at various industry conferences and to analysts, and possessed the power and authority to control the contents of those representations to the market. Because of their positions and access to material non-public information available to them, each of these Defendants knew that the adverse facts specified herein had not been disclosed to, and were being concealed from, the investing public, and that the positive representations which were being made were then materially false and/or misleading. Thus, the Individual Defendants had the opportunity to commit the fraudulent acts alleged herein. Accordingly, the Individual Defendants are responsible for the accuracy of the public reports and releases detailed herein and are therefore primarily liable for the representations contained therein.

IV. SUBSTANTIVE ALLEGATIONS

A. Company Background

28. Alkermes describes itself as a "fully integrated, global biopharmaceutical company that applies its scientific expertise and proprietary technologies to research, develop and commercialize . . . pharmaceutical products that are designed to address unmet medical needs of patients in major therapeutic areas." Alkermes possesses more than 20 commercial drug products including (i) proprietary products such as Aristada (schizophrenia) and Vivitrol (alcohol and opioid dependence); and (ii) products using Alkermes' proprietary technologies, such as Risperdal Consta (schizophrenia and bipolar I disorder), Invega Sustenna (schizophrenia and schizoaffective disorder), Xeplion (schizophrenia), Invega Trinza (schizophrenia), Trevicta (schizophrenia), Ampyra (treatment to improve walking in patients with MS), and Bydureon (type 2 diabetes).

Alkermes is headquartered in Dublin, Ireland, and has facilities and offices in Waltham, Massachusetts; Athlone, Ireland; and Wilmington, Ohio. As of February 2017, Alkermes had approximately 1,750 full-time employees, with a significant number of its management and professional employees having prior experience with pharmaceutical, biotechnology, or medical product companies.

B. The FDA Drug Approval Process

29. The FDA is responsible for, among other things, protecting public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices. Generally, when a company develops a drug, it conducts animal laboratory testing anywhere from a few years to more than five years prior to making an Investigational New Drug application ("IND") to the FDA. An IND is based on the results of the animal laboratory testing, and includes a description of the drug's composition and manufacturing process. The IND also outlines what the sponsor of a new drug proposes for human testing in clinical trials. The FDA then reviews the IND to ensure that the proposed clinical trials do not place potential human subjects at unreasonable risk of harm.

30. If the IND is granted, the investigative drug enters the following three phases of clinical trials:

i. Phase 1 emphasizes safety, and typically involves 20 to 80 healthy volunteers. The goal of Phase 1 is to determine the most frequent side effects, and how the drug is metabolized and excreted. The latter is determined through pharmacokinetic and pharmacodynamic testing and analysis.

ii. Phase 2 emphasizes efficacy, or effectiveness, and typically involves a few dozen to 300 patient volunteers. The goal of Phase 2 is to obtain preliminary data on whether the drug works in people who have a certain disease or condition. For controlled trials, patients receiving the drug are compared with similar patients receiving a different treatment—usually a placebo, or a different drug. Safety continues to be evaluated, and short-term side effects are studied. At the end of Phase 2, the FDA and the sponsoring company

discuss how large-scale studies in Phase 3 will be done. Phase 2 may also determine the effective dose of the drug to be used in the Phase 3 studies.

iii. Phase 3 typically involves several hundred to 3,000 patients in clinics and hospitals who are monitored carefully to determine effectiveness and identify adverse reactions. The goal of Phase 3 is to gather more information about safety and effectiveness, study different populations and different dosages, and use the drug in combination with other drugs.

31. After the three clinical trial phases are complete, the FDA meets with the sponsoring company prior to the submission of an NDA in a "pre-NDA meeting." The sponsoring company then formally asks the FDA to approve a drug for marketing in the United States by submitting an NDA. The NDA includes all animal and human data and analyses of the data, as well as information about how the drug behaves in the body and how it is manufactured.

32. The FDA has 60 days after an NDA is received to decide whether to file the NDA so it can be reviewed. The FDA may refuse to file the NDA and instead issue an RTF letter, which notifies the applicant that a major deficiency, or major deficiencies, exist(s) in the application. The RTF letter also gives the applicant the opportunity to amend its application so that a complete review can be conducted by the FDA. If the FDA decides to file the NDA, an FDA review team is assigned to evaluate the sponsor's research on the drug's safety and effectiveness. Occasionally, the FDA calls on advisory committees, which provide the FDA with independent opinions and recommendations from outside experts on applications to market new drugs. Once the review is complete, the FDA will either approve the NDA or issue a complete response letter rejecting the application.

C. Development of ALKS 5461

33. ALKS 5461 is an opioid combination product containing buprenorphine and samidorphan, intended to be used to treat MDD. If approved, ALKS 5461 would have been the first drug in an entirely new class of drugs to treat MDD, as no other opioids have yet been formally

evaluated for the treatment of depression.

34. ALKS 5461 has been under development for at least eight years, and Alkermes had a pre-IND meeting with the FDA regarding the drug on February 17, 2011. Initially, Alkermes envisioned ALKS 5461 as a treatment for cocaine dependence as well as MDD. In its Form 10-K for fiscal year 2011, filed May 18, 2012, Alkermes characterized ALKS 5461 as "a combination of [samidorphan] (an oral opioid modulator) and buprenorphine" that it was developing to be a non-addictive therapy for both the treatment of MDD in patients who have an inadequate response to standard antidepressant therapies, as well as for the treatment of cocaine dependence.

35. On June 11, 2011, Alkermes filed an IND with the FDA for the use of ALKS 5461 for the treatment solely of cocaine dependence. The IND was based on a "randomized, double-blind, multidose, placebo-controlled phase 1 clinical study" which assessed the "safety, tolerability and pharmacodynamic effects of the combination of [samidorphan] and buprenorphine when administered alone, and in combination as ALKS 5461, to 12 opioid-experienced users." In its Form 10-K for fiscal year 2011, Alkermes reported that the Phase 1 clinical study showed that ALKS 5461 was "generally well-tolerated" and that "sublingual administration of [samidorphan] effectively blocked the agonist effects of buprenorphine." The Form 10-K also noted that Alkermes was initiating a "Phase 1b study" of ALKS 5461 that targeted only cocaine dependence and was funded through a $2.4 million grant from the National Institute on Drug Abuse ("NIDA"). The results of this Phase 1b study were expected in mid-calendar year 2012.

36. On April 8, 2011, Alkermes filed an IND with the FDA for the use of ALKS 5461 for the treatment of MDD and subsequently, in January 2012, Alkermes announced positive results from a Phase 1/Phase 2 study of ALKS 5461 in 32 patients with MDD who did not adequately respond to standard antidepressant therapies, compared to placebos. Alkermes disclosed:

> In the study, ALKS 5461 was shown to significantly reduce depressive symptoms, as measured by the Hamilton Depression Rating Scale (HAM-D17; a standard, clinician-assessed measure of depression severity), in patients who received ALKS 5461 for the seven-day treatment period. In addition, data from the study showed that ALKS 5461 was generally well tolerated.

37. Based on this Phase 1/Phase 2 study, Alkermes initiated a "randomized, double-blind, multicenter, placebo-controlled Phase 2 study to evaluate the efficacy and safety of ALKS 5461 when administered once daily for four weeks in approximately 130 patients with MDD who have inadequate response to antidepressant therapy." The results of this Phase 2 study were expected in the first half of 2013.

38. The Phase 2 study was completed in April 2013, and Alkermes announced that the study had positive results:

> Preliminary topline results from the study showed that ALKS 5461 significantly reduced depressive symptoms across a range of standard measures including the study's primary outcome measure, the Hamilton Depression Rating Scale (HAM-D17), the Montgomery-Åsberg Depression Rating Scale (MADRS) and the Clinical Global Impression-Severity Scale (CGI-S). ALKS 5461 was generally well tolerated. Based on these results, as well as the positive Phase 1/2 results previously reported, Alkermes plans to request a meeting with the FDA and to advance ALKS 5461 into a pivotal development program. Data from this phase 2 study will be presented at a scientific meeting in May 2013.

39. On April 30, 2013, Alkermes submitted a request for feedback from the FDA "regarding the nonclinical and clinical requirements needed to support an overall Controlled Substances Act (CSA) scheduling recommendation for [buprenorphine and samidorphan], and on the adequacy of the samidorphan data package." Alkermes also abandoned ALKS 5461 as a treatment for cocaine dependence: in its Form 10-K for fiscal year 2012, filed May 23, 2013, Alkermes revised its description of ALKS 5461 and omitted mention of cocaine dependence, simply describing ALKS 5461 as "a proprietary investigational medicine with a novel mechanism

for the treatment of major depressive order."

40. In October 2013, Alkermes announced that it had "successfully completed [its] End-of-Phase 2 interactions with the FDA and that the FDA had granted ALKS 5461 Fast Track status for the adjunctive treatment of MDD in patients with an inadequate response to standard therapies," further noting that "Fast Track is a process designed to facilitate the development, and expedite the review of drugs to treat serious conditions with the potential to address an unmet medical need." Alkermes anticipated that Phase 3 would begin in the first quarter of 2014, and that this "pivotal" clinical program would "include three core phase 3 efficacy studies and is expected to enroll a total of approximately 1,500 patients with MDD who have had an inadequate response to standard therapies." With respect to the Phase 3 studies, Alkermes announced that "[t]he primary efficacy endpoint for all phase 3 studies will be the change in Montgomery-Åsberg Depression Rating Scale ("MADRS") scores from baseline. The pivotal program will also evaluate remission as a secondary endpoint. In addition to the three core efficacy studies, the program will also include studies to evaluate the long-term safety, pharmacokinetic profile, titration schedule and human abuse liability of ALKS 5461."

D. The FDA's Concerns

41. In late 2013, Alkermes requested an end-of-Phase 2 meeting. In advance of the meeting the FDA provided written responses to Alkermes' background package in which, unbeknownst to investors, the FDA conveyed concerns regarding Alkermes' planned SPCD analyses of ALKS 5461. Specifically, the FDA conveyed concerns to Alkermes in preliminary meeting comments about the planned SPCD analysis, stating that "although the proposed SPCD appears to be reasonable, ***there has been no analytical proof for the validity of associated***

statistical analyses when there are missing data" (emphasis added).[1] In short, while the FDA voiced no objection to SPCD in a proof-of-concept study (*i.e.*, an exploratory development stage aiming to show that the drug had some of the desired clinical activity, suitable at the Phase 1 stage), the FDA advised the Company to provide an SAP and seek feedback prior to initiating the trial if it intended to use the study to support an efficacy claim (*i.e.*, to prove that the drug was safe and effective for the purposes of a Phase 3 study). Alkermes withdrew its meeting request after receiving the FDA's preliminary responses, stating that the FDA's preliminary responses were sufficient and representing to the FDA that the SPCD analysis it used during its Phase 2 study was only intended to be used as a proof-of-concept study, and not to establish efficacy.

42. Despite this clear negative feedback received from the FDA calling into question Alkermes' clinical analyses of ALKS 5461, Alkermes continued to issue highly positive statements regarding the drug's developmental program. For instance, in its Form 10-K for fiscal year 2014 filed on February 24, 2015, Alkermes provided extensive information regarding its clinical program, stating:

> In March 2014, we announced the initiation of the pivotal clinical development program for ALKS 5461. The comprehensive pivotal program, named Focused On Results With A Rethinking of Depression ("FORWARD"), includes a total of twelve studies, including three core phase 3 efficacy studies and nine supportive studies. We announced initiation of two core efficacy studies in June 2014, and announced initiation of the third core efficacy study in July 2014. The core efficacy studies are designed to evaluate the safety and efficacy of ALKS 5461 as adjunctive treatment in patients with MDD. The FORWARD pivotal program will also include studies to evaluate the long-term safety, dosing, pharmacokinetic profile and human abuse liability of ALKS 5461. ***The three core efficacy studies will utilize state-of-the-art design methodologies intended to reduce the impact of clinically***

[1] These concerns were laid out in the FDA's briefing document for the "Psychopharmacologic Drugs Advisory Committee (PDAC) and Drug Safety and Risk Management (DSaRM) Advisory Committee Meeting," released October 30, 2018 (the "Briefing Document").

> ***meaningful placebo response***. Data from these three core efficacy studies are expected in 2016.
>
> In January 2015, we announced topline results from FORWARD-1, one of a series of supportive clinical studies in the FORWARD phase 3 pivotal program designed to evaluate the safety and tolerability of two titration schedules of ALKS 5461. ***Data from FORWARD-1 confirmed the safety and tolerability of ALKS 5461 in both titration schedules evaluated—one-week and two-week dose escalation schedules. These findings were consistent with the safety and tolerability profile seen in the phase 2 study of ALKS 5461 completed in 2013 in which ALKS 5461 met its primary endpoint,*** met key secondary endpoints and demonstrated significant reduction in depressive symptoms versus placebo. In addition, the exploratory efficacy analyses showed that ALKS 5461 reduced depressive symptoms from baseline in patients who received either of the two titration schedules. These data support the one-week titration schedule being utilized in the core phase 3 efficacy studies in the FORWARD program.

(emphasis added).

43. Nowhere in these disclosures regarding ALKS 5461 did Alkermes indicate, in any way, that the FDA had told Alkermes that the methods Alkermes used for the "phase 2 study of ALKS 5461 completed in 2013 in which ALKS 5461 met its primary endpoint" (*i.e.*, using the SPCD analysis), and to which Alkermes drew a successful comparison for purposes of the FORWARD-1 study, were problematic for the purposes of supporting an efficacy claim—one of the goals of a Phase 2 study.

44. The FDA continued to express explicit concerns regarding the clinical analyses for ALKS 5461 in future meetings. In fact, Alkermes proceeded to conduct ***Phase 3*** studies and on May 12, 2015, Alkermes requested a meeting to discuss and reach agreement on its SAPs for those Phase 3 studies. On July 24, 2015, the FDA provided a written response to Alkermes' meeting request background package, stating, "***[w]e would like to reiterate that we haven't endorsed any analytical method for SPCD in a confirmatory trial setting***. We are continuing making efforts in

further understanding its pros and cons from a regulatory perspective. You are encouraged to collect efficacy data from both stages. ***However, we may determine the efficacy based on data from only Stage 1 if analysis associated with this novel design is still unsettled by the time of your NDA filing***" (emphasis added). Thus, the FDA told Alkermes, yet again, that it questioned and did not approve of the methods Alkermes was using to support its efficacy claims in its Phase 2 and 3 clinical programs.

45. Despite this clear disapproval, Alkermes continued to paint a rosy picture of the developmental progress for ALKS 5461's clinical program and omit in its disclosures the explicit concerns expressed by the FDA multiple times since at least late 2013. For instance, in its Form 10-K for the 2015 fiscal year, filed February 25, 2016, Alkermes disclosed its ALKS 5461 progress as follows:

> In October 2013, the FDA granted Fast Track status for ALKS 5461 for the adjunctive treatment of MDD in patients with inadequate response to standard antidepressant therapies.
>
> In January 2015, we announced topline results from FORWARD-1, one of a series of supportive clinical studies in the FORWARD phase 3 pivotal program designed to evaluate the safety and tolerability of two titration schedules of ALKS 5461. ***Data from FORWARD-1 confirmed the safety and tolerability of ALKS 5461 in both titration schedules evaluated—one-week and two-week dose escalation schedules. These findings were consistent with the safety and tolerability profile seen in the phase 2 study of ALKS 5461 completed in 2013.*** In addition, the exploratory efficacy analyses showed that ALKS 5461 reduced depressive symptoms from baseline in patients who received either of the two titration schedules. These data supported the one-week titration schedule being utilized in the phase 3 efficacy studies in the FORWARD program. In December 2015, we also announced positive topline results from a human abuse potential study of ALKS 5461.
>
> In January 2016, we announced the topline results of FORWARD-3 and FORWARD-4, two phase 3 clinical studies of ALKS 5461 in MDD. Neither of the two studies met the prespecified primary efficacy endpoint, which compared ALKS 5461 to placebo on the

> change from baseline on the Montgomery-Åsberg Depression Rating Scale ("MADRS").
>
> FORWARD-4 tested two dose levels of ALKS 5461 (2mg/2mg and 0.5mg/0.5mg) compared to placebo. ***There was a clear trend toward efficacy with the 2mg/2mg dose of ALKS 5461 on the primary endpoint, and post hoc analyses achieved statistical significance for the entire 2mg/2mg dose group on the MADRS endpoint. Based on these analyses, we believe that FORWARD-4 provides supportive evidence of the efficacy of ALKS 5461 in the treatment of MDD.*** FORWARD-3 tested ALKS 5461 (2mg/2mg) compared to placebo. Placebo response was greater than that observed in FORWARD-4 and no treatment effect of ALKS 5461 was observed.
>
> * * *
>
> ***In the case of a clear positive outcome for FORWARD-5, we will consult with the FDA to determine whether the evidence provided by it and the previously completed successful, randomized, placebo-controlled phase 2 study, together with supportive evidence from FORWARD-4, collectively could provide substantial evidence of efficacy for ALKS 5461 for the adjunctive treatment of MDD***.

(emphasis added).

46. Thus, Alkermes yet again failed to convey any of the instances of negative feedback received from the FDA which questioned Alkermes' fundamental use of SPCD for its proposed Phase 3 efficacy evaluation.

47. On September 26, 2016, Alkermes met with the FDA to share preliminary results from Studies 205 ("FORWARD-4") and 206 ("FORWARD-3"), which were purportedly conducted for Phase 3 purposes. Both studies had failed to meet the prespecified primary endpoint—*i.e.*, the outcome, based on a drug's expected effects, that establishes the effectiveness, and/or safety features, of the drug in order to support regulatory action. In short, failure to meet the prespecified endpoint indicated that both studies failed to demonstrate the drug's efficacy.

48. On February 13, 2017, the FDA and Alkermes met yet again for a Type C meeting

(a meeting generally requested by the company to discuss the development and review of a product). The FDA, again, raised several red flags both in written responses provided in advance of the meeting, and during the meeting itself. For instance, and as disclosed in its October 2018 Briefing Document, the FDA's written responses stated that it generally "d[id] not accept major changes, such as revising the primary efficacy measures, in the late stage of a clinical trial" and that "that the primary endpoint and duration of the efficacy period for Stage 2 were changed very late in the course of the study"; that it had not accepted MADRS-6 as a primary efficacy endpoint for a clinical trial, and that it was concerned that MADRS-6 omitted "diagnostically and clinically important aspects of depression"; and that it "d[id] not agree with the strategy of comparing the baseline MADRS-6 or MADRS-10 scores to the average of the [MADRS-6 or MADRS-10] scores from Week 3 to the end of the efficacy period."

49. Thus, the FDA clearly indicated, yet again, that it did not agree with Alkermes' clinical analyses, including the revision of primary efficacy measures, the use of MADRS-6 as a primary efficacy endpoint, and the averaging of MADRS-6 and of MADRS-10 scores over time during the efficacy period. And yet again, Alkermes continued to omit any mention of the FDA's concerns and disagreements with the Company's methodologies, now expressed consistently and numerous times over several years, and in increasingly harsher terms. Alkermes' 2016 Form 10-K, filed February 17, 2017, characterized its ALKS 5461 progress as follows:

> In January 2016, we announced the topline results of FORWARD-3 and FORWARD-4 from the FORWARD (Focused on Results With a Rethinking of Depression) pivotal program. Neither study met the prespecified primary efficacy endpoint, which compared ALKS 5461 to placebo on the change from baseline on the 10-item Montgomery-Åsberg Depression Rating Scale ("MADRS-10") total scores. FORWARD-4, which tested two dose levels of ALKS 5461 (2mg/2mg and 0.5mg/0.5mg) compared to placebo, ***showed a clear trend toward efficacy with the 2mg/2mg dose of ALKS 5461 on the primary endpoint, and post hoc analyses achieved statistical***

> ***significance for the 2mg/2mg dose group on the MADRS-10 endpoint. Based on these analyses, we believe that FORWARD-4 provides supportive evidence of the efficacy of ALKS 5461 for the adjunctive treatment of MDD in patients with an inadequate response to standard antidepressant therapies***. FORWARD-3 tested ALKS 5461 (2mg/2mg) compared to placebo. Placebo response was greater than that observed in FORWARD-4 and no treatment effect of ALKS 5461 was observed.
>
> In October 2016, we announced positive topline results from FORWARD-5, a phase 3 randomized, double-blind, multicenter, placebo-controlled, sequential parallel comparison design study of ALKS 5461 in MDD from the FORWARD pivotal program***. ALKS 5461 2mg/2mg met the prespecified primary endpoint of significantly reducing depression scores compared to placebo, as measured by the 6-item Montgomery-Åsberg Depression Rating Scale ("MADRS-6")***. ALKS 5461 2mg/2mg also demonstrated statistically significant reductions in MADRS-10 scores compared to placebo. The 1mg/1mg dose of ALKS 5461 showed improvement in depressive symptoms in the study, but did not separate significantly from placebo. FORWARD-5 was conducted in two sequential stages: Stage 1 was 5 weeks in duration, and Stage 2 was 6 weeks. ***In Stage 1, the average change from baseline depression scores was calculated for weeks 3 through 5. For Stage 2, the average change from baseline was calculated for weeks 3 through 6. The results of Stages 1 and 2 were then averaged***. Depression scores were assessed using MADRS-6 and MADRS-10. MADRS-6, a subscale of the MADRS-10 assessment tool for depression, focuses on the core symptoms of depression. The most common adverse events for ALKS 5461 observed in the FORWARD efficacy studies included nausea, constipation and dizziness.
>
> ***Based on the results of FORWARD-5, the supportive evidence from FORWARD-4 and the successful phase 2 study of ALKS 5461, we recently met with the FDA's Division of Psychiatric Products at a Type C meeting to discuss ALKS 5461***. We will request a pre-NDA meeting with the FDA and plan to submit the New Drug Application ("NDA") for ALKS 5461 in the second half of 2017.

(emphasis added).

50. Despite specifically referencing the Type C meeting with the FDA, Alkermes yet again concealed the FDA's strongly negative comments from its investors regarding Alkermes'

revisions of primary efficacy measures late in the clinical trial, use of SPCD for efficacy purposes, use of MADRS-6 as a primary efficacy endpoint, and averaging of MADRS-6/MADRS-10 scores during the efficacy period.

51. On March 3, 2017, Alkermes submitted a preliminary Breakthrough Therapy Designation Request. Breakthrough Therapy Designation is "a process designed to expedite the development and review of drugs that are intended to treat a serious condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint." The FDA has indicated that in order for a Breakthrough Therapy Designation Request to be granted, preliminary clinical evidence should generally show a "clear advantage" over available therapy.

52. The FDA denied Alkermes' request, again stating that the FDA "had not yet determined whether the MADRS-6 was an acceptable endpoint," and that "any statistical significance in the phase 3 study results depended on post hoc analyses." Importantly, the FDA explained that "[a]lthough post hoc analyses of trials that fail on their prospectively specified endpoints may be useful for generating hypotheses for future testing, they do not yield definitive results. The results of such analyses can be biased because the choice of analyses can be influenced by a desire for success. . . . Consequently, ***post hoc analyses by themselves cannot establish effectiveness***. Also, additional endpoints that have not been pre-specified or evaluated with adjustment for multiplicity when required cannot, in general, be used to demonstrate an effect of the drug, even in successful studies" (emphasis added). If "any statistical significance in the phase 3 study results depended on *post hoc* analyses" and "*post hoc* analyses by themselves cannot establish effectiveness[,]" it clearly follows that the FDA would not consider the phase 3 results to establish effectiveness.

53. On April 24, 2017, Alkermes submitted a dossier on MADRS-6 to the FDA. After evaluating the submission, the FDA confirmed that the FDA's initial concerns were correct, and that MADRS-6 could not replace MADRS-10 for use as a primary endpoint because it excludes concepts that are relevant and important in treating MDD. Importantly, MADRS-6 excluded "reduced sleep," "reduced appetite," "concentration difficulties," and "suicidal thoughts" from its analysis. Furthermore, results of a factor analysis on MADRS-10 suggested that the four items removed were not redundant with the six items retained. This was a major problem for Alkermes, as many of its efficacy datasets were predicated on MADRS-6 only. However, yet again, Alkermes continued to conceal the FDA's concerns and criticisms of its methodologies in its regulatory filings, in earnings calls with analysts, and at conferences with analysts, as detailed *infra* in Section VI.

54. On July 24, 2017, Alkermes had a pre-NDA meeting with the FDA. During this meeting, the FDA informed Alkermes that any analyses of MADRS-6 scores would be considered ***exploratory only***—in short, alerting Alkermes that analyses of MADRS-6 scores would not be considered sufficient for, or even relevant to, NDA approval.

V. THE TRUTH EMERGES

A. The January 21, 2016 Announcement

55. On January 21, 2016, Alkermes issued a press release, attached to a Form 8-K filed the same day, announcing that although the first two of its three Phase 3 efficacy studies failed to meet their prespecified primary efficacy endpoints, the studies achieved "statistical significance" through "*post hoc* analyses." Industry analysts interpreted the reference to "*post hoc*" analysis—the means by which Alkermes claimed to have reached "statistical significance" despite the failure to meet primary efficacy endpoints—to refer to SPCD, which Alkermes had disclosed by at least late 2013 as one of the methods to be used in its efficacy studies. However, the public was yet

unaware that the FDA had, on multiple occasions, and as early as late 2013, expressed significant concerns to the Company regarding (and had specifically not authorized) the use of SPCD in the ALKS 5461 trials. Had the general public known that Alkermes had already agreed with the FDA that the SPCD analysis used during its "successful" Phase 2 study was only intended to be used as a proof-of-concept study, and not to establish efficacy, it would not have been surprised, or at least not as surprised, by the failure of the two Phase 3 studies to achieve their prespecified primary efficacy endpoints using standard, approved statistical analyses.

56. Analysts reacted negatively to the disclosure of the results of the Phase 3 efficacy studies; J.P. Morgan, in an analyst report titled "Depressing Outcome for '5461; Still See Meaningful LT Value in ALKS But Stepping to Sidelines For Now" noted that "FORWARD-4 showed a clear trend towards benefit but ended up being a near miss that, ***according to management, would have hit if using different statistical methods***" (emphasis added).

57. The market reacted sharply to the partial corrective disclosure that the studies did not meet their "prespecified primary efficacy endpoint" and that *post hoc* analysis was necessary to show efficacy: the Company's stock price dropped ***44.24***% from a closing price of $60.42 on January 20, 2016, to close at $33.69 on January 21, 2016, on volume of 12,467,289 shares, more than ***five times*** Alkermes' average volume during the month of January.

58. Notwithstanding the new information concerning the results of the ALKS 5461 Phase 3 efficacy studies revealed on January 21, 2016, the full truth regarding ALKS 5461's clinical development program was not revealed at that time, as Defendants continued to hide the FDA's skepticism and concerns regarding Alkermes' use of SPCD in its studies from the general public for over two more years. As a result, Alkermes common stock continued to trade at artificially inflated prices.

B. The April 2, 2018 RTF Letter

59. On January 31, 2018, Alkermes submitted its final portion of the NDA; approximately two months later, on April 2, 2018, Alkermes announced that it had received an RTF letter from the FDA regarding its NDA for ALKS 5461. In its April 2, 2018 press release, Alkermes disclosed that "the FDA has taken the position that it is unable to complete a substantive review of the regulatory package, based on insufficient evidence of overall effectiveness for the proposed indication, and that additional well-controlled clinical trials are needed prior to the resubmission of the NDA for ALKS 5461. In addition, the FDA has requested the conduct of a bioavailability study to generate additional bridging data between ALKS 5461 and the reference listed drug, buprenorphine." Alkermes stated that it "strongly disagree[d] with the FDA's conclusions and plans to appeal the FDA's decision," including seeking immediate guidance by requesting a "Type A meeting with the FDA to determine appropriate next steps and what additional information may be required to resubmit the NDA."[2] In its April 2, 2018 call discussing the RTF letter, Defendant Pops went even further, stating, "While we expected there to be questions during the review process, ***in none of these interactions did FDA raise concerns***, which would have let [*sic*] us to expect an RTF" (emphasis added). Notably, Defendant Pops' statement went beyond merely failing to disclose prior FDA concerns, and actively denied knowledge of their existence. Defendant Pops also effectively admitted that had one known of those FDA concerns, they "would have let [*sic*] [one] to expect an RTF."

60. Analysts were shocked and reacted negatively to the revelation of the problems underlying the RTF and to the RTF itself. Notably, analysts would not have been surprised by the RTF had they known of the FDA's concerns, which "would have let [*sic*] [one] to expect" the

[2] A Type A meeting is a meeting necessary for an otherwise stalled product development program to proceed.

RTF. That same day, for example, Cantor Fitzgerald issued an analyst report noting that the FDA response stood "in stark contrast to a comment by the CEO on 2Q17 results conference call. . . . ***[W]e believe investors may have been led to believe that FDA viewed the ALKS 5461 data potentially adequate for approval***. That the FDA has asked for additional clinical studies strongly calls into question such an assumption, in our opinion" (emphasis added).

61. J.P. Morgan also issued an analyst report the same day noting the FDA's "relatively extreme" language regarding questions around effectiveness and need for additional data, and "completely removed the product from [J.P. Morgan's] model pending additional updates." In a separate update, J.P. Morgan stated that "[t]he RTF for 5461 is clearly not a good start. This letter also appears to be particularly bad with comments around overall effectiveness (unusual for an RTF) and the need for additional clinical trials." Morgan Stanley's analyst report similarly stated that "***RTF on 5461 NDA is a negative surprise*** following Alkermes' Feb 14 [2018] guidance call which included an assumption of sales rep hiring in 2H:18" (emphasis added).

62. As the significance of Alkermes' partial disclosures was absorbed by the market, the Company's stock price dropped ***22%*** from a closing price of $57.96 on March 29, 2018, to close at $45.23 on April 2, 2018, on volume of 8,053,845 shares, approximately ***ten times*** Alkermes' average volume during the prior month of March.

C. The October 30, 2018 FDA Briefing Document in Advance of the November 1, 2018 Meeting of the Advisory Committees

63. On October 30, 2018, the FDA released the Briefing Document regarding ALKS 5461's NDA, in which the FDA publicly revealed, for the first time, the negative feedback it had continued to give Alkermes since early 2011 including, among other things:

i. Regarding the February 17, 2011 pre-IND meeting:

64. Upon hearing that Alkermes wished to use SPCD for its Phase 2 trial, the FDA

indicated that it did not think SPCD was suitable for a proof-of-efficacy trial, and would only be suitable for a proof-of-concept study. The FDA further stated that it "strongly encouraged the Applicant to provide a detailed statistical analysis plan (SAP) and seek feedback prior to initiating the trial if they intended to use the study to support an efficacy claim." The FDA further noted that Alkermes "did not follow our advice in study design" with respect to the provision of evidence of efficacy for both samidorphan and buprenorphine, and thus "did not complete the full factorial study for safety reasons noted."

ii. Regarding the October 2013 FDA written responses:

65. Upon receiving Alkermes' background package for an end-of-Phase 2 meeting, which described Alkermes' planned Phase 3 studies, the FDA again expressed concerns about the planned SPCD analyses through written preliminary responses prior to the meeting (as discussed *supra* in ¶ 41):

> From a statistical perspective, although the proposed SPCD appears to be reasonable, ***there has been no analytical proof for the validity of associated statistical analyses when there are missing data***. In the cited Chen et al. paper, the type I error rates were estimated by simulation. Without theoretical proof, it is not guaranteed that the type I error rate will be controlled, especially in scenarios where there are extensive dropouts. ***Since statistical validity of the methods associated with this novel design is not yet clear when there are missing data, it will be a matter of review whether or not efficacy demonstration can primarily rely on this method***. We note that you have pre-specified the MMRM approach as outlined by Chen et al. as the primary analysis and a few sensitivity analyses. To further assess the impact of missing data, you should propose sensitivity analyses that do not require the MAR (missing at random) assumption and provide details in the Statistical Analysis Plan.

(emphasis added).

iii. Regarding the July 2015 FDA written responses:

66. In July 2015, in response to Alkermes' background package in advance of a

meeting to discuss its SAPs for two of its three Phase 3 studies, Studies 205 (FORWARD-4) and 206 (FORWARD-3), the FDA again provided written responses (as discussed *supra* in ¶ 44), noting:

> ***We would like to reiterate that we haven't endorsed any analytical method for SPCD in a confirmatory trial setting***. We are continuing making efforts in further understanding its pros and cons from a regulatory perspective. You are encouraged to collect efficacy data from both stages. ***However, we may determine the efficacy based on data from only Stage 1 if analysis associated with this novel design is still unsettled by the time of your NDA filing***.
>
> Because of the limited time available for review of submissions via a meeting category, we can only provide general guidance on the proposed questions. If there is any change in protocol or stand-alone SAP, we advise that you submit it (including tracked changes and/or a detailed list of changes) separately from a meeting package.

(emphasis added).

iv. Regarding the September 26, 2016 Meeting

67. On September 26, 2016, Alkermes met with the FDA to share preliminary results from Studies 205 (FORWARD-4) and 206 (FORWARD-3). In this meeting, Alkermes "acknowledged that neither study met its prespecified primary endpoint and inquired about any additional analyses that could be conducted. The Agency had no recommendations but acknowledged that the additional analyses the Applicant already conducted could be informative for subsequent studies." In addition, Alkermes "presented some additional analyses that they said would inform modifications to the other ongoing short-term phase 3 study that was Study 207." Alkermes submitted an amendment to the SAP and protocol for Study 207 (also called "FORWARD-5") on September 19, 2016, which "changed the primary efficacy endpoint from change from baseline to end-of-treatment on the MADRS-10 to three primary endpoints to be evaluated in a hierarchical fashion," including (i) using MADRS-6 instead of MADRS-10, (ii) changing the primary endpoint and duration of the efficacy period, and (iii) comparing the baseline

scores to the average of the scores from Week 3 to the end of the efficacy period.

68. These amendments were submitted too late to be discussed at the September 26, 2016 meeting, and were ultimately discussed during a February 13, 2017 guidance meeting. In advance of the February 13, 2017 meeting, the FDA provided the following written responses clearly indicating that they did not approve of any of the proposed changes (as discussed *supra* in ¶ 48):

> 1. ***In general, we do not accept major changes, such as revising the primary efficacy measures, in the late stage of a clinical trial. It appears that the primary endpoint and duration of the efficacy period for Stage 2 were changed very late in the course of the stud***y.
>
> 2. ***We have not previously accepted the MADRS-6 as a primary efficacy endpoint for a clinical trial.*** Before accepting this instrument as primary endpoint in a trial intended to support product registration, we would need data on the validity and reliability of the instrument, and clear documentation of how the biometric properties of the MADRS-6 compare to the MADRS-10. ***On face, we have concerns that the MADRS-6 omits diagnostically and clinically important aspects of depression.***
>
> 3. ***We do not agree with the strategy of comparing the baseline MADRS-6 or MADRS-10 scores to the average of the scores from Week 3 to the end of the efficacy period.*** We note that the averaging of the change in MADRS-6 or MADRS-10 scores tends to obscure a possible dropoff in drug efficacy after the first few weeks of treatment. In Study 205, the change in MADRS-10 scores reached a peak at Week 3. In Study 207, the change in MADRS-6 and MADRS-10 scores both reached a peak at Week 4. It is important for us to know whether the drug has an effect that persists until the end of the study. ***We recommend using a single efficacy measure at the end of the study, and not an average over multiple time periods, as the primary efficacy endpoint.***
>
> 4. With the protocol amendment for Study 207, the efficacy period in Stage 1 is now different in duration from the efficacy period in Stage 2. This adds some complexity to the comparison of data from the two SPCD stages.

v. Regarding the March 2017 Request for Breakthrough Therapy Designation

69. In the Briefing Document, the FDA disclosed that it had informed Alkermes, in response to its March 3, 2017 Breakthrough Therapy Designation request, that because the FDA had not yet determined that MADRS-6 was an acceptable endpoint, and because any statistical significance in the Phase 3 study results depended on *post hoc* analyses, the FDA could not grant Breakthrough Therapy Designation.

vi. Regarding 2017 Evaluation of MADRS-6

70. The FDA notified Alkermes, during its July 24, 2017 pre-NDA meeting, that "the MADRS-6 was not fit for purpose" and "could not replace the MADRS-10 for use as a primary endpoint because it excludes concepts that are relevant and important in MDD," including "Reduced Sleep, Reduced Appetite, Concentration Difficulties, and Suicidal Thoughts," and because results of a factor analysis on MADRS-10 suggested that the four items removed were not redundant with the six items retained. At the pre-NDA meeting, the FDA further noted that these four missing items are "core features of depression" and "can't be excluded from an endpoint in a trial that is designed to assess anti-depressant efficacy."

D. The November 1, 2018 FDA Advisory Committees' Rejection of the NDA

71. On November 1, 2018, the FDA Advisory Committees voted 21 to 2 against the approval of ALKS 5461. Analysts expressed surprise at the information that they recognized had been withheld by Alkermes. For example, in a report that day, Credit Suisse wrote, "Extent of Differences Between FDA and Company Surprising: . . . It was surprising to us today to hear the amount of disagreement the FDA has on fundamental issues related to the ALKS 5461 program such as how the studies should have been designed and how many of the trials were actually positive and supportive of approval. We are also somewhat surprised by the relative optimism the Alkermes team still maintained for ALKS 5461 despite what were clearly significant objections that must have been voiced by the FDA during the development and review process." In response,

the price of Alkermes common stock plummeted ***7.57%*** from a closing price of $40.83 on October 31, 2018 (trading was halted on November 1, 2018), to $37.74 on November 2, 2018, for a loss of $480 million in market capitalization.

VI. FALSE AND MISLEADING STATEMENTS

A. The July 2014 Form 8-K, Form 10-Q, Press Release, and Earnings Call

72. On July 31, 2014, the Company filed its Form 10-Q for the quarter ended June 30, 2014, signed by Defendants Pops and Frates, stating:

> ALKS 5461 is a proprietary combination of samidorphan and buprenorphine that we are developing for the treatment of major depressive disorder ("MDD") in patients who have an inadequate response to standard antidepressant therapies. In March 2014, we announced the initiation of the pivotal clinical development program for ALKS 5461. The comprehensive pivotal program, named FORWARD (Focused On Results With A Rethinking of Depression), includes a total of 12 studies, including three core phase 3 efficacy studies and nine supportive studies. . . . The FORWARD pivotal program will include studies to evaluate the long-term safety, dosing, pharmacokinetic profile and human abuse liability of ALKS 5461. ***The three core efficacy studies will utilize state-of-the-art methodologies*** intended to reduce the impact of clinically meaningful placebo response. Data from these three core efficacy studies are expected in 2016.

(emphasis added).[3]

73. The bolded statements referenced above contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading. Specifically, the bolded statement *"[t]he three core efficacy studies will utilize state-of-the-art methodologies*," called SPCD (the methodology used for Alkermes' "three core efficacy studies" for Phase 3) a "state-of-the-art methodology," but blatantly omitted that SPCD was never proven to be a validated method of statistical analysis, and the FDA had, on

[3] All statements alleged to be false and misleading have been bolded throughout this section.

multiple occasions, expressed significant concerns regarding, and explicitly not authorized, the use of SPCD in the Phase 3 efficacy trials.

74. Alkermes and Defendants Pops and Frates knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made because, as discussed *supra* in ¶¶ 41 and 64-65, at the February 17, 2011 pre-IND meeting, the FDA informed Alkermes that it did not think SPCD was suitable for a proof-of-efficacy trial, and in October 2013, the FDA again expressed significant concerns regarding the use of SPCD in the clinical testing for ALKS 5461.

75. Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, 18 U.S.C. § 1350 ("SOX"), Defendants Pops and Frates certified the July 2014 Form 10-Q, stating that "information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company."

76. In addition, Defendants Pops and Frates certified the 2014 Form 10-Q pursuant to Section 302 of SOX, stating that:

> 1. I have reviewed this annual report on Form 10-Q of Alkermes plc;
>
> 2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
>
> 3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
>
> 4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and

internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

77. These certifications contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading. Pops and Frates knew, or recklessly disregarded, that the July 2014 Form 10-Q contained material misstatements and omissions regarding the FDA's significant concerns surrounding the use of SPCD in the clinical testing for ALKS 5461, based on skepticism and criticism Alkermes received from the FDA as described *supra* in ¶¶ 41 and 64-65.

78. That same day, July 31, Alkermes held a conference call with securities analysts to discuss Alkermes' 2014 second quarter financial results. During the conference call, Defendant Pops stated:

> Next is 5461, our novel drug candidate for major depressive disorder, which has fast track designation from the FDA and is moving very rapidly in development. ***With yesterday's announcement of the initiation of the FORWARD-5 study, all three core efficacy studies in the FORWARD are now underway.***
>
> These studies will evaluate the efficacy and safety of 5461 as an injunctive treatment in patients suffering from major depressive disorder who have an inadequate response to commonly prescribed drugs. ***We are encouraged that [site in]*** [sic] ***initiation is progressing ahead of our expectations*** and will look forward to updating you on our progress in this important program.

(emphasis added).

79. The bolded statements referenced above contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading. Specifically, the bolded statements "*all three core efficacy studies in the FORWARD are now underway*" and "*[w]e are encouraged that . . . initiation is progressing ahead of our expectations*" blatantly omitted that the FDA had, on multiple occasions, informed Alkermes that it did not think SPCD was suitable for a proof-of-efficacy trial, and conveyed significant concerns regarding the use of SPCD in clinical testing for ALKS 5461.

80. Alkermes and Defendant Pops knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made because, as discussed *supra* in ¶¶ 41 and 64-65, at the February 17, 2011 pre-IND meeting, the FDA informed Alkermes that it did not think SPCD was suitable for a proof-of-efficacy trial, and in October 2013, the FDA again expressed significant concerns regarding the use of SPCD in the clinical testing for ALKS 5461.

B. The October 2014 Earnings Call

81. On October 29, 2014, Alkermes held a conference call with securities analysts to discuss Alkermes' 2014 third quarter financial results. During the conference call, Defendant Pops stated:

> ***We're now entering a data-rich period over the next few months in which we're going to gain a clearer picture of the opportunities ahead of us***. To provide some context, let's take as an example ALKS 5461, our novel balanced neuromodulator product candidate for the treatment of major depressive disorder. ***A year and a half ago, we reported successful Phase 2 results*** which exemplified the way that data from highly informative studies can create a value inflection point for the company if they provide truly meaningful insights into the therapeutic value of a product candidate. As you know based on these data ALKS 5461 has rapidly evolved and today is a fast-track candidate being evaluated in a comprehensive pivotal program.
>
> * * *
>
> Remember that we've described the forward program, ***the overall pivotal program for 5461 as being quite comprehensive. It's anchored by these three core efficacy studies that we've talked about that mirror the SPCD, but it's also got a series of other studies. The one that just completed is one of those that provides very meaningful data,*** and you can look forward to us presenting data from the results of it and other studies over the course of the next several months.

(emphasis added).

82. The bolded statements referenced above contained material misstatements and/or

omitted to state material facts required therein or necessary to make the statements contained therein not misleading. Specifically, the bolded statement "*[w]e're now entering a data-rich period over the next few months in which we're going to gain a clearer picture of the opportunities ahead of us. . . . we reported successful Phase 2 results*" failed to disclose that Alkermes had agreed with the FDA that this so-called "successful" Phase 2 study was to be used as a proof-of-concept study only, and not to establish efficacy (*i.e.*, an exploratory development stage suitable for Phase 1, not Phase 2). Further, the bolded statement "*the overall pivotal program for 5461 . . . [is] anchored by these three core efficacy studies that we've talked about that mirror the SPCD, [and t]he one that just completed is one of those that provides very meaningful data*" omitted that the FDA had, on multiple occasions, conveyed skepticism and concerns regarding the use of SPCD in the clinical development program for ALKS 5461.

83. Alkermes and Defendant Pops knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made because, as discussed *supra* in ¶¶ 41 and 64-65, at the February 17, 2011 pre-IND meeting, the FDA informed Alkermes that it did not think SPCD was suitable for a proof-of-efficacy trial, and in October 2013, the FDA again expressed significant concerns regarding the use of SPCD in the clinical testing for ALKS 5461.

C. The November 2014 Credit Suisse Healthcare Conference

84. On November 11, 2014 at the Credit Suisse Healthcare Conference, Defendant Pops stated:

> So there's a major unmet need for well-tolerated oral medicines with new mechanism of action and that's what 5461 is designed to do. We had a very robust Phase 2 program like I said in the opening comment. ***This was about running a well-powered modern state-of-the-art study in depression designed to minimize the placebo response that characterizes many anti-depressive studies***.

> I won't take you through the design, you've all seen this many times before at this point, this was over a year ago now, ***using a method called Sequential Parallel Comparison Design, which is two parallel phases in a study where we minimize the placebo response, we saw robust efficacy.*** Importantly, in patients who are currently taking SSRI's and SNRI's, people who are on conventional therapy who are not getting adequate clinical relief, we're testing to see that when we add on top of that 5461 whether they begin to respond and indeed they did. ***And we saw -- this is the primary endpoint in our Phase 3 studies as in Phase 2, the MADRS which is the, which is a, scale for measuring depression, you saw major reductions in those scales in both stages of the study driving significant P values and this is what we're doing in Phase 3 is replicating these, this, design***.
>
> So this drug was granted fast-track status by FDA when we sent the submission in to begin the Phase 3 program and what that does for us is it helps us to qualify for priority review when we're done and has more frequent interactions with the FDA during the course of the development program and we started this very ambitious program called the forward program in Q1 of 2014 and now it's rolling in multiple sites and in multiple threshold of multiple countries.

(emphasis added).

85. The bolded statements referenced above contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading. Specifically, the bolded statement "*[t]his was about running a well-powered modern state-of-the-art study in depression designed to minimize the placebo response that characterizes many anti-depressive studies*," by referring to SPCD as a "state-of-the-art methodology," blatantly omitted that SPCD was never proven to be a validated method of statistical analysis, and the FDA had, on multiple occasions, expressed significant concerns regarding, and explicitly not authorized, the use of SPCD in the Phase 3 efficacy trials. Further, the bolded statement "*using a method called Sequential Parallel Comparison Design . . . we saw robust efficacy*" again omitted that SPCD was never proven to be a validated method of statistical

analysis, and the FDA had, on multiple occasions, expressed significant concerns regarding, and explicitly not authorized, the use of SPCD in the Phase 3 efficacy trials. Finally, the bolded statement "*this is the primary endpoint in our Phase 3 studies as in Phase 2, the MADRS which is the, which is a, scale for measuring depression, you saw major reductions in those scales in both stages of the study driving significant P values and this is what we're doing in Phase 3 is replicating these, this, design*" neglected to mention that unlike Phase 2, where the Company used MADRS-10 as the primary endpoint, in Phase 3 the Company changed the primary endpoint to MADRS-6.

86. Alkermes and Defendants Pops knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made because, as discussed *supra* in ¶¶ 41 and 64-65, at the February 17, 2011 pre-IND meeting, the FDA informed Alkermes that it did not think SPCD was suitable for a proof-of-efficacy trial, and in October 2013, the FDA again expressed significant concerns regarding the use of SPCD in the clinical testing for ALKS 5461.

D. The December 2014 NASDAQ OMX Investor Program

87. On December 2, 2014, Defendant Pops provided substantial detail regarding Alkermes' SPCD analysis during the NASDAQ OMX Investor Program:

> ***We demonstrated in clinical trials very powerful efficacy in precisely this patient population***; those who are failing to achieve adequate responses on SSRI's so when we talk about our placebo controlled studies the placebo group is getting active medication in the form of SSRI's and ***we're demonstrating efficacy on top of that and we got a fair amount of attention for the innovativeness of the clinical trial design which we're replicating in Phase 3 which is called the Sequential Parallel Comparison Design*** which is a way of minimizing placebo affect which is endemic to studies of patients with depression.

(emphasis added).

88. The bolded statements referenced above contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading. Specifically, the bolded statement "*[w]e demonstrated in clinical trials very powerful efficacy*" was false; Alkermes had never proven "very powerful efficacy" in any of the studies conducted by Alkermes at that time, when reviewed by the FDA. Alkermes had agreed with the FDA that its Phase 2 study was *not* to be used to establish efficacy (*see* ¶ 41 *supra*). In addition, the statement "*we got a fair amount of attention for the innovativeness of the clinical trial design which we're replicating in Phase 3 which is called the Sequential Parallel Comparison Design*" omitted that the FDA had, on multiple occasions, conveyed skepticism and concerns regarding the use of SPCD in the clinical development program for ALKS 5461.

89. Alkermes and Defendant Pops knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made because, as discussed *supra* in ¶¶ 41 and 64-65, at the February 17, 2011 pre-IND meeting, the FDA informed Alkermes that it did not think SPCD was suitable for a proof-of-efficacy trial, and in October 2013, the FDA again expressed significant concerns regarding the use of SPCD in the clinical testing for ALKS 5461.

E. The 2014 Form 10-K

90. On February 24, 2015, the Company filed its Form 10-K with the SEC for the fiscal year ended December 31, 2014, signed by Defendants Pops and Frates. The statements in the Form 10-K discussed below contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading.

91. Under Part I, Item 1, under the subheading "ALKS 5461," the Form 10-K stated:

> In March 2014, we announced the initiation of the pivotal clinical development program for ALKS 5461. The comprehensive pivotal program, named Focused On Results With A Rethinking of

> Depression ("FORWARD"), includes a total of twelve studies, including three core phase 3 efficacy studies and nine supportive studies. We announced initiation of two core efficacy studies in June 2014, and announced initiation of the third core efficacy study in July 2014. The core efficacy studies are designed to evaluate the safety and efficacy of ALKS 5461 as adjunctive treatment in patients with MDD. The FORWARD pivotal program will also include studies to evaluate the long-term safety, dosing, pharmacokinetic profile and human abuse liability of ALKS 5461. ***The three core efficacy studies will utilize state-of-the-art design methodologies intended to reduce the impact of clinically meaningful placebo response***. Data from these three core efficacy studies are expected in 2016.

(emphasis added).

92. The bolded statements referenced above contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading. Specifically, the bolded statement "*[t]he three core efficacy studies will utilize state-of-the-art design methodologies intended to reduce the impact of clinically meaningful placebo response"* called SPCD (the methodology used for Alkermes' "three core efficacy studies" for Phase 3) a "state-of-the-art methodology," but blatantly omitted that SPCD was never proven to be a validated method of statistical analysis, and the FDA had, on multiple occasions, expressed significant concerns regarding, and explicitly not authorized, the use of SPCD in the Phase 3 efficacy trials.

93. Alkermes and Defendants Pops and Frates knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made because, as discussed *supra* in ¶¶ 41 and 64-65, at the February 17, 2011 pre-IND meeting, the FDA informed Alkermes that it did not think SPCD was suitable for a proof-of-efficacy trial, and in October 2013, the FDA again expressed significant concerns regarding the use of SPCD in the clinical testing for ALKS 5461.

94. Pursuant to Section 906 of SOX, Defendants Pops and Frates certified the 2014 Form 10-K, stating that "[t]he information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company."

95. In addition, Defendants Pops and Frates certified the 2014 Form 10-K pursuant to Section 302 of SOX, attaching substantially the same certifications as set forth *supra* in ¶ 76. These certifications contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading. Pops and Frates knew, or recklessly disregarded, that the 2014 Form 10-K contained material misstatements and omissions regarding ALKS 5461, based on strong criticisms Alkermes received from the FDA regarding the drug's clinical trial processes as described *supra* in ¶¶ 41 and 64-65.

F. The April 2015 Earnings Call

96. On April 30, 2015, Alkermes held a conference call with securities analysts to discuss Alkermes' 2014 first quarter financial results. During the conference call, Defendant Pops stated:

> ***Based on the compelling data from the Phase II program***, and the fast-track designation from FDA in hand, ***last year we initiated the comprehensive [FORWARD] pivotal program with the goal of conducting a robust series of studies to support US registration*** and wide utilization of this medicine.

(emphasis added).

97. The bolded statements referenced above contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading. Specifically, the bolded statement "*[b]ased on the compelling data from the Phase II program . . . last year we initiated the comprehensive [FORWARD] pivotal program with the goal of conducting a robust series of studies to support US registration*" omitted that the referenced "compelling data" and the "comprehensive [FORWARD] pivotal program" was based

on SPCD, a study design regarding which the FDA had, on multiple occasions, conveyed skepticism and concerns.

98. Alkermes and Defendant Pops knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made because of the reasons discussed *supra* in ¶¶ 41 and 64-65.

G. The July 2015 Earnings Call

99. On July 30, 2015, Alkermes held a conference call with securities analysts to discuss Alkermes' 2015 second quarter financial results. During the conference call, Defendant Pops stated:

> ALKS 5461, the three studies I would describe is the shades of the same color. ***They all employ the sequential parallel comparison design we've talked about before, which we saw in Phase 2 to minimize the placebo response so there all conducted in these two phases, with re-randomization of the placebo non-responders which were -- we think is a really important design feature***.

100. The bolded statements referenced above contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading. Specifically, the bolded statement "*the three studies . . . all employ the sequential parallel comparison design we've talked about before, which we saw in Phase 2 to minimize the placebo response so there all conducted in these two phases . . .*" omitted that FDA had, on multiple occasions—the most recent at this time being ***six days prior*** to this earnings call—conveyed skepticism and concerns regarding the use of SPCD in the clinical development program for ALKS 5461.

101. Alkermes and Defendant Pops knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made because, in addition to the reasons discussed *supra* in ¶¶ 41 and 64-65, in July 2015, the FDA

reiterated that it had not endorsed "any analytical method for SPCD in a confirmatory trial setting" and that the FDA "may determine the efficacy based on data from only Stage 1 if analysis associated with this novel design is still unsettled" by the time the NDA is filed.

102. Analysts relied on Alkermes' misrepresentation that the use of SPCD was valid and authorized by the FDA; on December 16, 2015, Morgan Stanley's analyst report noted, regarding ALKS 5461, that "[w]e also expect positive Phase 3 results from three trials in 2016. Our confidence is based on Phase 2 validation of both the mechanisms and the innovative clinical trial design (sequential parallel comparison design). Mgmt [*sic*] stated on the 3Q call, '*We're on track to have data from FORWARD-4 in early Q1 2016, data from FORWARD-3 later in that same quarter, and data from FORWARD-5 in Q3 2016.*'" (emphasis in original).

H. The January 2016 Form 8-K and Press Release

103. On January 21, 2016, as discussed *supra* in ¶ 55, Alkermes issued a press release announcing that two of its three Phase 3 efficacy studies failed to meet their prespecified efficacy endpoints, but were able to reach statistical significance through *post hoc* analysis. The press release was also filed with the SEC as an exhibit to a Form 8-K signed by Defendant Frates. The press release stated:

> Alkermes plc (NASDAQ: ALKS) today announced preliminary topline results from FORWARD-3 and FORWARD-4, the first two of three phase 3 efficacy studies to read out from the comprehensive FORWARD pivotal program for ALKS 5461. Neither of the two studies met the prespecified primary efficacy endpoint, which compared ALKS 5461 to placebo on the change from baseline on the Montgomery—Åsberg Depression Rating Scale (MADRS). . . . There was a clear trend toward efficacy with the 2mg/2mg dose of ALKS 5461 on the primary endpoint, ***and* post hoc *analyses achieved statistical significance for the entire 2mg/2mg dose group on the MADRS endpoint***. Based on these analyses, Alkermes believes that FORWARD-4 provides supportive evidence of the efficacy of ALKS 5461 in the treatment of major depressive disorder.

(emphasis added).

104. The bolded statements referenced above contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading. Specifically, the bolded statement "*post hoc analyses achieved statistical significance for the entire 2mg/2mg dose group"* omitted that the FDA had conveyed skepticism and concerns regarding SPCD, the method used for the *post hoc* analyses to achieve statistical significance.

105. Alkermes and Defendant Frates knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made because, as discussed *supra* in ¶¶ 41, 64-65, and 101, (i) at the February 17, 2011 pre-IND meeting, the FDA informed Alkermes that it did not think SPCD was suitable for a proof-of-efficacy trial; (ii) in October 2013, the FDA again expressed significant concerns regarding the use of SPCD; and (iii) in July 2015, the FDA reiterated that it had not endorsed "any analytical method for SPCD in a confirmatory trial setting" and that the FDA "may determine the efficacy based on data from only Stage 1 if analysis associated with this novel design is still unsettled" by the time the NDA is filed.

I. The February 2016 Leerink Partners Global Healthcare Conference

106. On February 11, 2016, Defendant Pops stated at the Leerink Partners Global Healthcare Conference:

> The third study, FORWARD-5, is currently underway. And what we expect to do is to update you on the timing of the completion of FORWARD-5 on our earnings call, which will be February 25. Right now, the thinking in the Company is we're trying to determine whether we want to increase the sample size of that study at all or modestly to increase the power of it. We may not. ***We actually -- we're pretty happy with the design and the conduct of the study.*** What we will certainly do is modify the pre-specified statistical

> analysis plan, which is fine to do. So our statisticians are working on that and we'll do that.
>
> * * *
>
> I guess I don't think of the FDA as ever being flexible per se. I think they respond to data. ***And the study designs that we're using have been talked about with FDA and these are these sequential parallel comparison designs or versions thereof. And it's about looking for truth***. And the nice thing about the FORWARD program in the three studies that we're running, coupled with what we've done in Phase 2, is we've been -- look, there's a large number of exposures in randomized controlled settings, a range of doses and a very consistent patient population. So I think we're really centering in on what is the truth.

(emphasis added).

107. The bolded statements referenced above contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading. Specifically, the bolded statements "*we're pretty happy with the design and the conduct of the study*" and "*the study designs that we're using have been talked about with FDA and these are the sequential parallel comparison designs or versions thereof. And it's about looking for truth"* completely omitted that, during the referenced discussions with the FDA regarding SPCD, the FDA had conveyed skepticism and concerns regarding the use of SPCD in the clinical development program for ALKS 5461.

108. Alkermes and Defendant Pops knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made because of the reasons discussed *supra* in ¶¶ 41, 64-65, and 101.

J. The 2015 Form 10-K

109. On February 25, 2016, the Company filed its Form 10-K with the SEC for the fiscal year ended December 31, 2015, signed by Defendants Pops and Frates. The statements in the Form

10-K discussed below contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading.

110. Under Part I, Item 1, under the subheading "ALKS 5461," the Form 10-K stated:

> In January 2016, we announced the topline results of FORWARD-3 and FORWARD-4, two phase 3 clinical studies of ALKS 5461 in MDD. Neither of the two studies met the prespecified primary efficacy endpoint, which compared ALKS 5461 to placebo on the change from baseline on the Montgomery-Åsberg Depression Rating Scale ("MADRS").
>
> FORWARD-4 tested two dose levels of ALKS 5461 (2mg/2mg and 0.5mg/0.5mg) compared to placebo. ***There was a clear trend toward efficacy with the 2mg/2mg dose of ALKS 5461 on the primary endpoint, and post hoc analyses achieved statistical significance for the entire 2mg/2mg dose group on the MADRS endpoint***. Based on these analyses, we believe that FORWARD-4 provides supportive evidence of the efficacy of ALKS 5461 in the treatment of MDD. FORWARD-3 tested ALKS 5461 (2mg/2mg) compared to placebo. Placebo response was greater than that observed in FORWARD-4 and no treatment effect of ALKS 5461 was observed.

(emphasis added).

111. The bolded statements referenced above contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading. Specifically, the bolded statement "*[t]here was a clear trend toward efficacy with the 2mg/2mg dose of ALKS 5461 on the primary endpoint, and post hoc analyses achieved statistical significance for the entire 2mg/2mg dose group on the MADRS endpoint*" omitted that the FDA had conveyed skepticism and concerns regarding SPCD, the method used for the *post hoc* analyses to achieve statistical significance.

112. Alkermes and Defendants Pops and Frates knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made because of the reasons discussed *supra* in ¶¶ 41, 64-65, and 101.

113. Pursuant to Section 906 of SOX, Defendants Pops and Frates certified the 2015 Form 10-K, stating that "[t]he information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company."

114. In addition, Defendants Pops and Frates certified the 2015 Form 10-K pursuant to Section 302 of SOX, attaching substantially the same certifications as set forth *supra* in ¶ 76. These certifications contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading. Pops and Frates knew, or recklessly disregarded, that the 2015 Form 10-K contained material misstatements and omissions regarding ALKS 5461, based on strong criticisms Alkermes received from the FDA regarding the drug's clinical trial processes as described *supra* in ¶¶ 41, 64-65, and 101.

K. The June 2016 Conference Call

115. On June 1, 2016, Defendant Ehrich stated during the Alkermes Conference Call to Discuss Data and Study Design from FORWARD-3 and FORWARD-4 Studies of ALKS 5461:

> Fourth, the central issue in the design of depression studies is seeking to minimize placebo response. It is well known and documented that increasing placebo response rates threaten the ability of clinical trials to demonstrate efficacy of antidepressants, and failed clinical trials occur frequently. Even among studies of FDA-approved antidepressants there's been an estimated 50% failure rate.
>
> ***To address the issue of placebo response, researchers at Harvard Medical School developed a clinical trial design called SPCD, Sequential Parallel Comparison Design. This design has been used in a number of successful studies in depression, including the second Phase II Study of ALKS-5461***. While all of the forward core efficacy studies used elements of SPCD, FORWARD-4 and the ongoing FORWARD-5 studies employed a classic SPCD structure. FORWARD-3 used a related but alternate design sharing certain common features

(emphasis added).

116. The bolded statements referenced above contained material misstatements and/or

omitted to state material facts required therein or necessary to make the statements contained therein not misleading. Specifically, the bolded statement "*[t]o address the issue of placebo response, researchers at Harvard Medical School developed a clinical trial design called SPCD, Sequential Parallel Comparison Design. This design has been used in a number of successful studies in depression, including the second Phase II Study of ALKS-5461*" omitted that the FDA had, on multiple occasions, conveyed skepticism and concerns regarding the use of SPCD in the clinical development program for ALKS 5461.

117. Alkermes and Defendant Ehrich knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made because of the reasons discussed *supra* in ¶¶ 41, 64-65, and 101.

L. The October 2016 Conference Call

118. On October 20, 2016, Defendant Ehrich stated during the Alkermes Conference Call to Discuss FORWARD-5 ALKS 5461 Data:

> This afternoon we announced positive topline results from FORWARD-5, and this is really exciting for us here at Alkermes. . . . In the study, ALKS 5461 achieved statistically significant efficacy on the primary endpoint of improvement in depression scores. The data are clear and ALKS 5461 behaved in a manner consistent with previous studies.
>
> * * *
>
> ***The study employed a sequential parallel comparison design or SPCD*** that was very similar in construct to what we used in the two previous studies, FORWARD-4, as well as the successful Phase 2 study which we refer to as Study 202. . . . The primary endpoint of an SPCD study is evaluated by averaging the results from Stage 1 and Stage 2.
>
> ***The FORWARD-5 study was positive***. The 2:2 dose of ALKS 5461 demonstrated statistically significant reductions in average MADRS-6 scores from baseline compared to placebo with a P value of 0.018. MADRS-6 measures the core symptoms of depression and was the prespecified primary endpoint.

* * *

> But what you are actually getting to is a very important point, which is that what ***we do see is study after study after study, we are seeing this consistent efficacy effect***. And that really adds to the overall assessment of the robustness of the finding of antidepressant activity with ALKS 5461.

(emphasis added).

119. The bolded statements referenced above contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading. Specifically, the bolded statement "*[t]he study employed a sequential parallel comparison design or SPCD . . . The FORWARD-5 study was positive*" omitted that the FDA had, on multiple occasions, conveyed skepticism and concerns regarding the use of SPCD in the clinical development program for ALKS 5461. Similarly, the statement "*we do see is study after study after study, we are seeing this consistent efficacy effect*" neglected to mention that the "consistent efficacy effect" was based on study designs that the FDA had specifically refused to endorse for that purpose.

120. Alkermes and Defendant Ehrich knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made because of the reasons discussed *supra* in ¶¶ 41, 64-65, and 101.

M. The November 2016 Form 10-Q and Earnings Call

121. On November 2, 2016, the Company filed its Form 10-Q for the quarter ended September 31, 2017, signed by Defendants Pops and Frates. The Form 10-Q stated:

> ***In October 2016, we announced positive topline results from FORWARD-5, a phase 3 randomized, double-blind, multicenter, placebo-controlled, sequential parallel comparison design study of ALKS 5461 in MDD from the FORWARD (Focused on Results With a Rethinking of Depression) pivotal program. ALKS 5461 2mg/2mg met the prespecified primary endpoint of significantly***

> ***reducing depression scores compared to placebo***, as measured by the 6-item Montgomery-Åsberg Depression Rating Scale ("MADRS-6"). ***ALKS 5461 2mg/2mg also demonstrated statistically significant reductions in the 10-item Montgomery-Åsberg Depression Rating Scale ("MADRS-10") scores compared to placebo***. The 1mg/1mg dose of ALKS 5461 showed improvement in depressive symptoms in the study, but did not separate significantly from placebo. The most commonly reported adverse events for ALKS 5461 in the FORWARD-5 study were nausea, dizziness and fatigue.

(emphasis added).

122. The bolded statements referenced above, and specifically the statement "*[i]n October 2016, we announced positive topline results from FORWARD-5, a phase 3 randomized, double-blind, multicenter, placebo-controlled, sequential parallel comparison design study of ALKS 5461 in MDD from the FORWARD (Focused on Results With a Rethinking of Depression) pivotal program. . . . ALKS 5461 2mg/2mg met the prespecified primary endpoint of significantly reducing depression scores compared to placebo . . . ALKS 5461 2mg/2mg also demonstrated statistically significant reductions in the 10-item Montgomery-Åsberg Depression Rating Scale ("MADRS-10") scores compared to placebo*" omitted that at multiple times the FDA had conveyed skepticism and concerns regarding the use of SPCD in the clinical development program for ALKS 5461, and that any referenced "positive topline results" were based on study designs that the FDA had specifically refused to endorse.

123. As discussed *supra* in ¶¶ 41, 64-65, and 101, Alkermes and Defendants Pops and Frates knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made.

124. Pursuant to Section 906 of SOX, Defendants Pops and Frates certified the November 2016 Form 10-Q, stating that "information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company."

125. In addition, Defendants Pops and Frates certified the November 2016 Form 10-Q pursuant to Section 302 of SOX, attaching substantially the same certifications as set forth *supra* in ¶ 76. These certifications contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading. Pops and Frates knew, or recklessly disregarded, that the November 2016 Form 10-Q contained material misstatements and omissions regarding ALKS 5461, based on the strong criticisms Alkermes received from the FDA regarding the drug as described *supra* in ¶¶ 41, 64-65, and 101.

126. That same day, Alkermes also held a conference call with securities analysts to discuss Alkermes' 2016 third quarter financial results. During the conference call, Defendant Pops stated:

> FORWARD-5 was a double-blind, placebo-controlled study that evaluated the safety, tolerability, and efficacy of two dose levels of ALKS 5461 in 407 subjects. ***The efficacy results from FORWARD-5 were clear and positive. So, the results from FORWARD-5 are clear and robust. So we believe that the positive FORWARD-5 study, taken together with the confirmatory results from our randomized controlled phase 2 study, the supportive data from the FORWARD-4 study that were reported earlier this year, and data from the collective 5461 clinical program provides substantial evidence of efficacy in support of a regulatory submission***. So as I said earlier, I think the robustness of the data -- of the consistency of the data -- is what is so striking. Any single study can be informative, but when you put them all together, that's where I think the power of the 5461 data set lies. Really, our meeting with FDA is to review the data from the entire FORWARD package and talk about our regulatory approach. This is a fast-track designating medicine. ***We've had multiple conversations with*** [sic] ***FDA about this medicine along the way, and we really consider it to be part of an ongoing update on our registration pathway for ALKS 5461***.

(emphasis added).

127. The bolded statements referenced above contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained

therein not misleading. Specifically, the bolded statements "*[t]he efficacy results from FORWARD-5 were clear and positive. So, the results from FORWARD-5 are clear and robust. So we believe that the positive FORWARD-5 study, taken together with the confirmatory results from our randomized controlled phase 2 study, the supportive data from the FORWARD-4 study that were reported earlier this year, and data from the collective 5461 clinical program provides substantial evidence of efficacy in support of a regulatory submission*" and "*We've had multiple conversations with FDA about this medicine along the way, and we really consider it to be part of an ongoing update on our registration pathway for ALKS 5461*" again omitted that during the referenced "multiple conversations with [*sic*] FDA," the FDA had conveyed skepticism and concerns regarding the use of SPCD in the clinical development program for ALKS 5461, and that the positive results were based on study designs that the FDA had specifically refused to endorse.

128. Alkermes and Defendant Pops knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made because of the reasons discussed *supra* in ¶¶ 41, 64-65, and 101.

N. The November 8, 2016 Credit Suisse Healthcare Conference

129. On November 8, 2016, Defendant Pops stated during the Credit Suisse Healthcare Conference:

> So, it's a fast track medicine, and we've had this large FORWARD-- what was called the FORWARD program, which was our multiple studies in Phase 3. ***And just last month we reported positive data from the last of those called FORWARD-5 that showed compelling and significant improvements in depression scores and an internal consistency and a replication of studies that we've seen in the past.***

(emphasis added).

130. The bolded statements referenced above contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained

therein not misleading. Specifically, the bolded statement "*[a]nd just last month we reported positive data from the last of those called FORWARD-5 that showed compelling and significant improvements in depression scores and an internal consistency and a replication of studies that we've seen in the past*" omitted that at multiple times the FDA had conveyed skepticism and concerns regarding the use of SPCD in the clinical development program for ALKS 5461, and that any referenced "positive data" and "compelling and significant improvements" were based on study designs that the FDA had specifically refused to endorse.

131. As discussed *supra* in ¶¶ 41, 64-65, and 101, Alkermes and Defendant Pops knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made.

O. The January 2017 JPMorgan Healthcare Conference

132. On January 10, 2017, Defendant Pops stated during the J.P. Morgan Healthcare Conference:

> With the FORWARD program now compete, we have developed a substantial registration package, with data from more than 20 studies in 1,500 patients. ***Data from these studies are remarkably consistent in terms of the efficacy, the safety, and the tolerability of ALKS 5461.*** We'll meet with the FDA later this quarter, probably in February, to share the data from the most recent efficacy studies and expect a pre-NDA meeting in Q2 followed by submission of the NDA at year-end for this Fast Track medicine**.**

(emphasis added).

133. The bolded statements referenced above contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading. Specifically, the statement "*[d]ata from these studies are remarkably consistent in terms of the efficacy, the safety, and the tolerability of ALKS 5461*" omitted that at multiple times the FDA had conveyed skepticism and concerns regarding the use of SPCD in the

clinical development program for ALKS 5461, and that any referenced positive results were based on study designs that the FDA had specifically refused to endorse.

134. As discussed *supra* in ¶¶ 41, 64-65, and 101, Alkermes and Defendant Pops knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made.

P. The January 2017 JPMorgan Healthcare Q&A

135. Following the above J.P. Morgan Healthcare Conference, on January 10, 2017, Defendant Pops stated during the J.P. Morgan Healthcare Q&A:

> ***So, the first meeting we wanted to request was what's called a Type C meeting, a guidance meeting, for February, where we want to carry on what we did, most recently in September, where we met with them and showed them the results of FORWARD-3 and FORWARD-4, and told them what our plan was for FORWARD-5***. So, now we'll go show them FORWARD-5 as well as the pooled analysis of FORWARD-4 and FORWARD-5, so they have a complete sense of the totality of the data that we've generated.
>
> * * *
>
> ***So, I think the nice thing about 5461's data is that it's so remarkably consistent across the multiple studies***. And it's the totality of the evidence that will be in the NDA, rather than any one particular study, that showed the consistency of the 2/2 dose across multiple studies, compared then to lower and higher doses that we tested in the context of the program as well. So, you can see the -- within the context of the program, doses that don't work; and within the same experiment, compare it to doses that -- a dose that does work.

(emphasis added).

136. The bolded statements referenced above contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading. Specifically, the bolded statement "*[s]o, the first meeting we wanted to request was what's called a Type C meeting, a guidance meeting, for February, where we want to*

carry on what we did, most recently in September, where we met with them and showed them the results of FORWARD-3 and FORWARD-4, and told them what our plan was for FORWARD-5" omitted that during the September meeting with the FDA, Alkermes had admitted to the FDA that neither study had met its prespecified primary endpoint. In addition, the bolded statement "*[s]o, I think the nice thing about 5461's data is that it's so remarkably consistent across the multiple studies*" omitted that at multiple times the FDA had conveyed skepticism and concerns regarding the use of SPCD in the clinical studies for ALKS 5461, and that any referenced "consistent" results were based on study designs that the FDA had specifically refused to endorse.

137. As discussed *supra* in ¶¶ 41, 64-65, and 101, Alkermes and Defendant Pops knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made.

Q. The 2016 Form 10-K

138. On February 17, 2017, the Company filed its Form 10-K with the SEC for the fiscal year ended December 31, 2016, signed by Defendants Pops and Frates. The statements in the Form 10-K discussed below contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading.

139. Under Part I, Item 1, under the subheading "ALKS 5461," the Form 10-K stated:

> In January 2016, we announced the topline results of FORWARD-3 and FORWARD-4 from the FORWARD (Focused on Results With a Rethinking of Depression) pivotal program. Neither study met the prespecified primary efficacy endpoint, which compared ALKS 5461 to placebo on the change from baseline on the 10-item Montgomery-Åsberg Depression Rating Scale ("MADRS-10") total scores. FORWARD-4, which tested two dose levels of ALKS 5461 (2mg/2mg and 0.5mg/0.5mg) compared to placebo, showed a clear trend toward efficacy with the 2mg/2mg dose of ALKS 5461 on the primary endpoint, and ***post hoc analyses achieved statistical significance for the 2mg/2mg dose group on the MADRS-10 endpoint.*** Based on these analyses, we believe that FORWARD-4 provides supportive evidence of the efficacy of ALKS 5461 for the

> adjunctive treatment of MDD in patients with an inadequate response to standard antidepressant therapies. FORWARD-3 tested ALKS 5461 (2mg/2mg) compared to placebo. Placebo response was greater than that observed in FORWARD-4 and no treatment effect of ALKS 5461 was observed.
>
> ***In October 2016, we announced positive topline results from FORWARD-5, a phase 3 randomized, double-blind, multicenter, placebo-controlled, sequential parallel comparison design study of ALKS 5461 in MDD from the FORWARD pivotal program. ALKS 5461 2mg/2mg met the prespecified primary endpoint of significantly reducing depression scores compared to placebo, as measured by the 6-item Montgomery-Åsberg Depression Rating Scale ("MADRS-6").*** ALKS 5461 2mg/2mg also demonstrated statistically significant reductions in MADRS-10 scores compared to placebo. The 1mg/1mg dose of ALKS 5461 showed improvement in depressive symptoms in the study, but did not separate significantly from placebo. ***FORWARD-5 was conducted in two sequential stages: Stage 1 was 5 weeks in duration, and Stage 2 was 6 weeks. In Stage 1, the average change from baseline depression scores was calculated for weeks 3 through 5. For Stage 2, the average change from baseline was calculated for weeks 3 through 6. The results of Stages 1 and 2 were then averaged. Depression scores were assessed using MADRS-6 and MADRS-10. MADRS-6, a subscale of the MADRS-10 assessment tool for depression, focuses on the core symptoms of depression.*** The most common adverse events for ALKS 5461 observed in the FORWARD efficacy studies included nausea, constipation and dizziness.
>
> Based on the results of FORWARD-5, the supportive evidence from FORWARD-4 and the successful phase 2 study of ALKS 5461, we recently met with the FDA's Division of Psychiatric Products at a Type C meeting to discuss ALKS 5461. We will request a pre-NDA meeting with the FDA and plan to submit the New Drug Application ("NDA") for ALKS 5461 in the second half of 2017.

(emphasis added).

140. The bolded statements referenced above contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading. Specifically, the bolded statement "*post hoc analyses achieved statistical significance for the 2mg/2mg dose group on the MADRS-10 endpoint*" omitted that the FDA had

conveyed skepticism and concerns regarding SPCD, the method used for the *post hoc* analyses to achieve statistical significance. In addition, the bolded statement "*[i]n October 2016, we announced positive topline results from FORWARD-5, a phase 3 randomized, double-blind, multicenter, placebo-controlled, sequential parallel comparison design study of ALKS 5461 in MDD from the FORWARD pivotal program"* omitted that at multiple times, the FDA had expressed significant concerns regarding, and had explicitly not authorized, the use of SPCD in the ALKS 5461 trials. Further, the bolded statement "*ALKS 5461 2mg/2mg met the prespecified primary endpoint of significantly reducing depression scores compared to placebo, as measured by [MADRS-6] . . . Depression scores were assessed using MADRS-6 and MADRS-10. MADRS-6, a subscale of the MADRS-10 assessment tool for depression, focuses on the core symptoms of depression*" omitted that at multiple times, including at the Type C meeting referenced above, the FDA specifically stated to Alkermes that it did not endorse MADRS-6 as a primary endpoint because it did not address four key concepts relevant and important to treating MDD: "reduced sleep," "reduced appetite," "concentration difficulties," and "suicidal thoughts." Finally, the bolded statement "*[i]n October 2016, we announced positive topline results from FORWARD-5 . . . [which] was conducted in two sequential stages . . . In Stage 1, the average change from baseline depression scores was calculated for weeks 3 through 5. For Stage 2, the average change from baseline was calculated for weeks 3 through 6. The results of Stages 1 and 2 were then averaged*" omitted that at the Type C meeting referenced above, the FDA specifically stated that it did not endorse Alkermes' strategy of comparing dose groups based on averaged MADRS-6 or averaged MADRS-10 scores over several weeks.

141. Alkermes and Defendants Pops and Frates knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements

were made because of the reasons discussed *supra* in ¶¶ 41, 64-65, and 101, and also because (i) in September 2016, the FDA notified Alkermes that, among other things, the FDA did not approve of the revision of primary efficacy measures, the use of MADRS-6 as a primary efficacy endpoint, and the averaging of MADRS-6/MADRS-10 scores during the efficacy period, and (ii) in the February 2017 Type C meeting, the FDA specifically stated to Alkermes that it did not endorse MADRS-6 as a primary endpoint, nor did it endorse Alkermes' strategy of comparing dose groups based on averaged scores over several weeks.

142. Pursuant to Section 906 of SOX, Defendants Pops and Frates certified the 2016 Form 10-K, stating that "[t]he information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company."

143. In addition, Defendants Pops and Frates certified the 2016 Form 10-K pursuant to Section 302 of SOX, attaching substantially the same certifications as set forth *supra* in ¶ 76. These certifications contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading. Pops and Frates knew, or recklessly disregarded, that the 2016 Form 10-K contained material misstatements and omissions regarding ALKS 5461, based on strong criticisms Alkermes received from the FDA regarding the drug's clinical trial processes as described *supra* in ¶¶ 41, 64-65, 101, and 141.

R. The March 2017 Cowen Health Care Conference

144. On March 7, 2017, Defendant Pops stated during the Cowen Health Care Conference that:

> We'll be presenting data from our pivotal study in a couple of months' time in May followed by the NDA submission. . . We've now run multiple studies to move from the theory, the neuroscience theory, to actually empirical results, five placebo-controlled studies, and this is the scorecard. Three of them positive . . . I don't think that there is an approved antidepressant therapy that hasn't had one or more failed studies due to high placebo response. This is – this

> comes with the turf when you're developing drugs in this patient population. ***So, we're quite confident in the dataset that we've developed. I often say the drug has revealed itself through these large numbers of studies. The data are quite comprehensive. And as you analyze the entire dataset, you can get quite comfortable of the safety and efficacy of this drug and the treatment of major depressive disorder.*** So, another critical part of the assessment of 5461 is its safety because, ultimately, FDA approval is a risk-benefit calculation. And there's two elements of the safety and tolerability that are focal for 5461. One is its overall profile, right? How well tolerated is this as a medicine for patients with depression? And the answer to that is very good. The other relates to this addictive potential. Have we indeed ablated the addictive potential of the opioid? And the nice thing about having such a large dataset is we can see very clearly that we've done that. . . . ***So, we really feel like the risk-benefit for this medicine is very much in favor of use of 5461***.

(emphasis added).

145. The bolded statements referenced above contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading. Specifically, the bolded statement "*as you analyze the entire dataset, you can get quite comfortable of the safety and efficacy of this drug and the treatment of major depressive disorder. . . . So we really feel like the risk-benefit for this medicine is very much in favor of use of 5461*" omitted that the FDA had not, at any point, determined that the dataset for efficacy evaluation was acceptable, and in fact had conveyed to Alkermes numerous times that it did not endorse significant portions of Alkermes' analyses, including the use of SPCD, the use of MADRS-6 as a primary endpoint, and the comparison of dose groups based on averaged MADRS-6 or MADRS-10 scores over several weeks.

146. As discussed *supra* in ¶¶ 41, 64-65, 101, and 141, Alkermes and Defendant Pops knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made.

S. The March 2017 Barclays Global Healthcare Conference

147. On March 14, 2017, Defendant Frates stated at the Barclays Global Healthcare Conference that:

> ***We get to see the whole data package, all 1500 patients, the safety data, all the studies that have been done. And one of the hallmarks of it is the consistency of effect. And so, as we've gone to show the FDA a little bit more data in the type C meeting. . . we feel as confident as we have coming out of that meeting as we did going in and we're still on track. . . .*** There is always a very strong placebo response in these studies and so separating from placebo is the coin of the realm. And I think the consistent separation from placebo is something that's hallmark of 5461. The other thing is that it is safe. (emphasis added).

148. The bolded statements referenced above, and specifically the statement *"[w]e get to see the whole data package, all 1,500 patients. And one of the hallmarks of [the data package] is the consistency of effect. And so, as we've gone to show the FDA a little bit more data in the type C meeting. . . we feel confident as coming out as much as we did going in and we're still on track*," omitted that (i) the FDA had not, at any point, determined that the dataset for efficacy evaluation was acceptable; (ii) some of the 1,500 patients were in studies utilizing MADRS-6, and did not meet the efficacy endpoint according to MADRS-10; (iii) the FDA had explicitly stated at the referenced Type C meeting that it did not endorse significant portions of Alkermes' analyses; and (iv) at multiple times, the FDA had expressed significant concerns regarding, and had explicitly not authorized, the use of SPCD in the ALKS 5461 trials.

149. As discussed *supra* in ¶¶ 41, 64-65, 101, and 141, Alkermes and Defendant Frates knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made.

T. The April 2017 Form 8-K, Form 10-Q, Press Release, and Earnings Call

150. On April 27, 2017, Alkermes issued a press release announcing its financial results

for the first quarter of 2017. The press release was also filed with the SEC as an exhibit to a Form 8-K signed by Defendant Frates. The April 27 press release highlighted the Company's purportedly bright outlook on ALKS 5461, stating that "our late stage pipeline continues to advance rapidly in 2017 with the planned New Drug Application submission for ALKS 5461 for the adjunctive treatment of major depressive disorder."

151. The same day, the Company filed its Form 10-Q for the quarter ended March 31, 2017, signed by Defendants Pops and Frates. The Form 10-Q reiterated that the NDA process for ALKS 5461 was going smoothly, stating:

> ***In February 2017, we met with the FDA's Division of Psychiatric Products at a Type C meeting to discuss ALKS 5461.*** We have requested a pre-NDA meeting with the FDA and plan to submit the NDA for ALKS 5461 in the second half of 2017.
>
> In April 2017, we announce plans to initiate a phase 3 study of ALKS 5461 in the second quarter of 2017. ***Study will use the MADRS and will include additional scales and endpoints where ALKS 5461 may have particular benefit.***

(emphasis added).

152. The bolded statements referenced above, and specifically the statements "*[i]n February 2017, we met with the FDA's Division of Psychiatric Products at a Type C meeting to discuss ALKS 5461" and "[s]tudy will use the MADRS and will include additional scales and endpoints where AKS 5461 may have particular benefit*" omitted that at multiple times, including at the Type C meeting referenced above, the FDA explicitly stated to Alkermes that (i) it did not endorse MADRS-6 as a primary endpoint because it did not address four key concepts relevant and important to treating MDD: "reduced sleep," "reduced appetite," "concentration difficulties," and "suicidal thoughts," and (ii) it did not endorse Alkermes' strategy of comparing dose groups based on averaged MADRS-6 or averaged MADRS-10 scores over several weeks.

153. As discussed *supra* in ¶¶ 41, 64-65, 101, and 141, Alkermes and Defendants Pops and Frates knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made.

154. Pursuant to Section 906 of SOX, Defendants Pops and Frates certified the April 2017 Form 10-Q, stating that "information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company."

155. In addition, Defendants Pops and Frates certified the April 2017 Form 10-Q pursuant to Section 302 of SOX, attaching substantially the same certifications as set forth *supra* in ¶ 76. These certifications contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading. Pops and Frates knew, or recklessly disregarded, that the April 2017 Form 10-Q contained material misstatements and omissions regarding ALKS 5461, based on the strong criticisms Alkermes received from the FDA regarding the drug as described *supra* in ¶¶ 41, 64-65, 101, and 141.

156. On April 27, 2017, Alkermes also held a conference call with securities analysts to discuss Alkermes' 2017 first quarter financial results. During the conference call, Defendant Pops stated:

> The approval of 5461 as an adjunctive agent in patients failing to get adequate clinical relief from first-line treatments, as measured by MADRS should just be the beginning. We're going to continue to expand the dataset supporting ALKS 5461's distinctive clinical profile through new clinical trials. . . . ***We are on track for submitting the NDA by years-end. There is a strong consensus that the drug is doing as intended and will be approvable in that indication***. So we will absolutely give feedback coming out of the pre-NDA meeting.

(emphasis added).

157. The bolded statements referenced above, and specifically the statement "*[w]e are*

on track for submitting the NDA by years-end. There is a strong consensus that the drug is doing as intended and will be approvable in that indication" omits that the FDA explicitly stated to Alkermes multiple times, as discussed *supra* in ¶¶ 41, 64-65, 101, and 141, and in denying Breakthrough Therapy Designation in March 2017, that it did not endorse significant portions of Alkermes' analyses, thus directly contradicting the statement that there is a "strong consensus that the drug is doing as intended" and the NDA package would be approved.

158. As discussed *supra* in ¶¶ 41, 64-65, 101, 141, and 157, Alkermes and Defendants Pops and Frates knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made.

U. The May 2017 Deutsche Bank Health Care Conference

159. On May 3, 2017, Defendant Frates stated during the Deutsche Bank Health Care Conference that "***5461 is a potential blockbuster***. I won't go into details of our clinical studies. Anybody who follows the company, looks at research can see the outcomes. They've not been all positive. . . . *We've had 3 placebo-controlled studies that are clearly positive****. . . . So the whole package together, we think, is*** [sic] ***will be able to get us approval through the FDA***." (emphasis added).

160. The bolded statements referenced above, and specifically the statement "*5461 is a potential blockbuster. . . So the whole package together, we think, is* [sic] *will be able to get us approval through the FDA*" omitted that the FDA explicitly stated to Alkermes numerous times that it had significant concerns regarding, and had explicitly not authorized, its clinical development program, thus giving Defendants no reasonable basis to state that the NDA package would likely be approved by the FDA. As discussed *supra* in ¶¶ 41, 64-65, 101, 141, and 157, Alkermes and Defendant Frates knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made.

V. The May 2017 Society of Biological Psychiatry Annual Meeting

161. On May 18, 2017, Defendant Ehrich stated during the Society of Biological Psychiatry Annual Meeting that:

> We incorporated 2 key elements in the statistical analysis plan. ***First, instead of relying on a single time point to determine the success or failure with an inherently variable measurement, we prespecified the primary endpoint of FORWARD-5 as the change in depression score from baseline to the average of the final weeks of the 2 stages. We believe the continuous measurement of efficacy across multiple time points is a more powerful and precise evaluation of a drug's efficacy profile.*** *Second, we chose to use the 6-item Montgomery-Asberg Depression Rating Scale, or MADRS-6, as our primary efficacy assessment.* ***MADRS-6 focuses on the core mood symptoms of depression and may provide a more precise measure of antidepressant activity for patients in adjunctive treatment settings.***
>
> * * *
>
> So to summarize, ***through the FORWARD development program, ALKS 5461 has demonstrated safety, tolerability and efficacy in the adjunctive treatment of MDD.*** We'll meet with the FDA for our scheduled pre-NDA meeting, and we're on track for our preparations for submitting the NDA by year-end.

(emphasis added).

162. The bolded statements referenced in the preceding paragraph, and specifically the statements "*[f]irst, instead of relying on a single time point to determine the success or failure with an inherently variable measurement, we prespecified the primary endpoint of FORWARD-5 as the change in depression score from baseline to the average of the final weeks of the 2 stages. We believe the continuous measurement of efficacy across multiple time points is a more powerful and precise evaluation of a drug's efficacy profile*"; "*MADRS-6 focuses on the core mood symptoms of depression and may provide a more precise measure of antidepressant activity for patients in adjunctive treatment settings*"; and "*through the FORWARD development program, ALKS 5461 has demonstrated safety, tolerability and efficacy in the adjunctive treatment of MDD*"

omitted that the FDA explicitly stated to Alkermes numerous times that (i) it did not endorse Alkermes' strategy of comparing dose groups based on averaged measurements over several weeks; (ii) it did not endorse MADRS-6 as a primary endpoint because that methodology did not address four key concepts relevant and important to treating MDD: "reduced sleep," "reduced appetite," "concentration difficulties," and "suicidal thoughts"; and (iii) it had significant concerns regarding, and had explicitly not authorized, the use of SPCD in the ALKS 5461 trials.

163. The statements referenced in the preceding paragraph also omitted that the FDA explicitly stated to Alkermes numerous times that it had significant concerns regarding its clinical development program, thus giving Defendants no reasonable basis to state that the NDA package would likely be approved by the FDA. As discussed *supra* in ¶¶ 41, 64-65, 101, 141, and 157, Alkermes and Defendant Ehrich knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made.

W. The June 2017 Jefferies Healthcare Conference

164. On June 6, 2017, Defendant Frates stated during the Jefferies Healthcare Conference that:

> [W]e have a broad clinical program, a number of Phase IIIs, over 1,500 patients with data. . . . ***And the overall program, we think, is very solid. So data from the FORWARD core efficacy studies have shown a consistent efficacy across those large Phase IIIs***. We've seen the same results very consistently. . . . ***And an important risk-benefit analysis that the regulators, the FDA is going to do, and we think we'll come out well in that process***.

(emphasis added).

165. The bolded statements referenced above, and specifically the statements "*the overall program, we think, is very solid. . . . data from the FORWARD core efficacy studies have shown a consistent efficacy across those large Phase IIIs"*; and "*an important risk-benefit analysis that the regulators, the FDA is going to do, and we think we'll come out well in that process*"

omitted that (i) the FDA had not, at any point, determined that the dataset for efficacy evaluation was acceptable; and (ii) the FDA explicitly stated to Alkermes numerous times that it had significant concerns with multiple elements of the clinical development program. As discussed *supra* in ¶¶ 41, 64-65, 101, 141, and 157, Alkermes and Defendant Frates knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made.

X. The June 2017 Goldman Sachs Global Healthcare Conference

166. On July 15, 2017, Defendant Pops stated during the Goldman Sachs Global Healthcare Conference that:

> ***[W]e and our statistical consultants and our key opinion leader consultants have a common view of this data, which is it's a very persuasive dataset showing the safety and efficacy of 5461***.
>
> * * *
>
> So it's truly the totality of the dataset. ***And we have analyzed it every which way you can, and we expect FDA to do the same. There's also clear evidence of dose response and there's also really beautiful tolerability. So ultimately, when you come down to the risk-benefit calculation, which is the ultimate decision that any regulatory body will make, you have to lay out what are –what's the evidence of the efficacy and what are the attendant risks associated with efficacy. And that balance, I think, is overwhelmingly in favor of the use of 5461.***

(emphasis added).

167. The bolded statements referenced above, and in particular the statements "*we and our statistical consultants and our key opinion leader consultants have a common view of this data, which is it's a very persuasive dataset showing the safety and efficacy of 5461"* and "*we have analyzed it every which way you can, and we expect FDA to do the same. There's also clear evidence of dose response . . . So ultimately, when you come down to the risk-benefit calculation,*

which is the ultimate decision that any regulatory body will make, you have to lay out what are – what's the evidence of the efficacy and what are the attendant risks associated with efficacy. And that balance, I think, is overwhelmingly in favor of the use of 5461" omitted that (i) the FDA had not, at any point, determined that the dataset for efficacy evaluation was acceptable; and (ii) the FDA explicitly stated to Alkermes numerous times that it had significant concerns with multiple elements of the clinical development program. As discussed *supra* in ¶¶ 41, 64-65, 101, 141, and 157, Alkermes and Defendant Pops knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made. Moreover, the statement "We've analyzed the data every which way and we expect FDA to do the same" is in direct contradiction to the FDA's repeated statements that it would ***not*** analyze the data "every which way." Instead, the FDA stated that it did not support certain analyses, including stating that it "do[es] not agree with the strategy of comparing the baseline MADRS-6 or MADRS-10 scores to the average of the scores from Week 3 to the end of the efficacy period."

Y. The July 2017 Form 8-K, Form 10-Q, and Earnings Call

168. On July 27, 2017, Alkermes issued a press release announcing its financial results for the second quarter of 2017. The press release was also filed with the SEC as an exhibit to a Form 8-K signed by Defendant Frates. The July 27 press release continued to highlight the Company's purportedly bright outlook on ALKS 5461, stating that "[f]ollowing a pre-NDA meeting with FDA for ALKS 5461 earlier this week, we are on track to begin rolling submission of the ALKS 5461 New Drug Application next month and expect to complete the submission by year-end 2017. We are excited to bring this important, potential, new proprietary medicine to patients struggling with major depressive disorder."

169. The same day, the Company filed its Form 10-Q for the quarter ended June 30, 2017, signed by Defendants Pops and Frates. The Form 10-Q again reiterated that the NDA process

for ALKS 5461 was going smoothly, stating:

> ***In February 2017 and July 2017, we met with the FDA's Division of Psychiatric Products at a Type C meeting and a pre-NDA meeting, respectively, to discuss ALKS 5461. We plan to submit the NDA for ALKS 5461 by the end of 2017.***
>
> In June 2017, we initiated Study 217, a phase 3b study of ALKS 5461 in patients suffering from MDD who have had an inadequate response to commonly prescribed drugs for depression. ***It uses the Montgomery-Åsberg Depression Rating Scale ("MADRS"),*** and will also include additional scales and endpoints related to social connection, anhedonia and resilience, which are regulated by endogenous opioid modulation and where ALKS 5461 may have particular benefit.

(emphasis added).

170. The bolded statements referenced above, and specifically the statements "*[i]n February 2017 and July 2017, we met with the FDA's Division of Psychiatric Products at a Type C meeting and a pre-NDA meeting, respectively, to discuss ALKS 5461. We plan to submit the NDA for ALKS 5461 by the end of 2017*" and "*[i]n June 2017, we initiated Study 217, a phase 3b study of ALKS 5461 . . . [which] uses the Montgomery-Åsberg Depression Rating Scale*" omitted that the FDA explicitly stated to Alkermes multiple times, including at the referenced Type C meeting and pre-NDA meeting, that the FDA did not endorse significant portions of Alkermes' analyses, including the use of MADRS-6 as a primary endpoint, as opposed to MADRS-10, because MADRS-6 did not address four key concepts relevant and important to treating MDD: "reduced sleep," "reduced appetite," "concentration difficulties," and "suicidal thoughts," and thus would consider any analyses of MADRS-6 scores as exploratory only (*i.e.*, analyses of MADRS-6 scores would not be considered sufficient for, or even supportive of, NDA approval).

171. Alkermes and Defendants Pops and Frates knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements

were made because, in addition to the events described *supra* in ¶¶ 41, 64-65, 101, 141, and 157, the FDA notified Alkermes during its July 24, 2017 pre-NDA meeting that MADRS-6 could not replace MADRS-10 for use as a primary endpoint.

172. Pursuant to Section 906 of SOX, Defendants Pops and Frates certified the July 2017 Form 10-Q, stating that "information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company."

173. In addition, Defendants Pops and Frates certified the July 2017 Form 10-Q pursuant to Section 302 of SOX, attaching substantially the same certifications as set forth *supra* in ¶ 76. These certifications contained material misstatements and/or omitted to state material facts required therein or necessary to make the statements contained therein not misleading. Pops and Frates knew, or recklessly disregarded, that the July 2017 Form 10-Q contained material misstatements and omissions regarding ALKS 5461, based on the strong criticisms Alkermes received from the FDA regarding the drug as described *supra* in ¶¶ 41, 64-65, 101, 141, 157, and 171.

174. The same day, Alkermes also held a conference call with securities analysts to discuss Alkermes' 2017 second quarter financial results. During the earnings call, Defendant Pops stated:

> Earlier this week, we passed a major milestone with the outcome of our pre-NDA meeting with FDA, which resulted in an agreement on our NDA submission content and timing. Based on that meeting, we plan to begin the rolling submission of the NDA for ALKS 5461 in August. . . . ***we're pleased with the outcome of this week's interaction and we're looking forward to entering the review phase, as we work to bring this important new medicine to patients***.

(emphasis added).

175. Notably, during the question and answer portion of the earnings call, an analyst at

J.P. Morgan asked about "FDA feedback on 5461 from your pre-NDA meeting . . . did they provide any thoughts or insight during the session on MADRS-6 or averaging? And in terms of the rolling filing itself, is there any one thing that is going to be the big gating factor here or is it just the overall size of the application?" In response, Defendant Pops stated:

> So on the 3 things that folks are asking us about, MADRS-6, averaging, SPCD, all these things, we got some clarity. ***So we now know that FDA intends to focus on MADRS-10 as the primary efficacy measure, which was the efficacy measure that was collected across all of our efficacy studies. For studies that evaluated MADRS-6, they will – indicated they will review the MADRS-6 DATA, but their primary analysis will be on MADRS-10. But as you know, we collected MADRS-10 in all the studies as well, so that's fine***. Regarding averaging, as you know, we believe that averaging is a more accurate way of capturing drug effect over time and it's central to our efficacy analysis, although we'll make all the data available for FDA to review in the NDA. ***So they can analyze the data however they choose to it.*** We didn't talk about averaging in this meeting, as we discussed it in the past, and we expected it to be a review issue, which is appropriate. ***SPCD studies are becoming the best practice in the development of new medicines for the treatment of major depressive disorder.*** I think you're seeing that broadly. That said, the 5461 NDA will be the first NDA based on SPCD efficacy analysis. ***So I think that the FDA is well-versed in SPCD and its potential utility in psychiatric trials and we discussed it with them for a number of years now. So I felt that we got what we wanted out of that interaction.***

(emphasis added).

176. Moreover, an analyst from Leerink Partners asked, "Now that the FDA is going to be primarily looking at the MADRS-10, I'm wondering if you could talk about how you think the FDA could be conceptualizing the data you've shown in terms of statistics? So specifically, I think the MADRS-10 was a secondary endpoint in FORWARD-5. It hit statistical significance, but does the way that they do the stats change because it was a secondary endpoint, but it's their primary focus in the data?" In response, Defendant Pops stated:

> ***[W]e're really quite indifferent to which they choose. We believe MADRS-6 is interesting from the point of view that it addresses core symptoms of mood,*** which in the adjunctive setting, when patients are receiving SSRIs, this is often the unresolved part of their depression, because the other medicines may be addressing sleep and appetite and things like that. ***So we and clinicians will continue to believe that MADRS-6 is important, but we're perfectly fine with analysis that focuses on MADRS-10.***

(emphasis added).

177. The bolded statements referenced above in ¶¶ 174-176, and specifically the statement "*SPCD studies are becoming the best practice in the development of new medicines for the treatment of major depressive disorder*" omitted that at multiple times, the FDA had expressed significant concerns regarding, and had explicitly not authorized, the use of SPCD in the ALKS 5461 trials, thus giving Defendants no reasonable basis to state that SPCD studies are "becoming the best practice." In addition, the statements "*we now know that FDA intends to focus on MADRS-10 as the primary efficacy measure . . . we're really quite indifferent to [whether the FDA chooses MADRS-10 or MADRS-6]. We believe MADRS-6 is interesting from the point of view that it addresses core symptoms of mood*"; and "*the FDA is well-versed in SPCD and its potential utility in psychiatric trials and we discussed it with them for a number of years now. . . . we got what we wanted out of that interaction*" omitted that at multiple times, including at the pre-NDA meeting specifically referred to above, the FDA explicitly stated to Alkermes that it had significant concerns with multiple elements of the clinical development program, including that (i) the FDA did not endorse MADRS-6 as a primary endpoint because it did not address four key concepts relevant and important to treating MDD: "reduced sleep," "reduced appetite," "concentration difficulties," and "suicidal thoughts," and thus would consider any analyses of MADRS-6 scores as exploratory only (*i.e.*, analyses of MADRS-6 scores would not be considered sufficient for, or even supportive of, NDA approval); (ii) the FDA did not endorse Alkermes' strategy of comparing

dose groups based on averaged MADRS-6 or averaged MADRS-10 scores over several weeks; and (iii) the FDA had not, at any point, determined that the dataset for efficacy evaluation was acceptable, and specifically questioned the use of data included because of the use of the SPCD analysis.

178. As discussed *supra* in ¶¶ 41, 64-65, 101, 141, 157, and 171, Alkermes and Defendant Pops knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made.

Z. The November 2017 Credit Suisse Healthcare Conference

179. On November 7, 2017, Defendant Frates stated during the Credit Suisse Healthcare Conference that:

> As we talked to our experts and experts in the field, ***the folks who see the data really understand that 5461 has the opportunity to be a really revolutionary medication because its going to be one - really, it's the first new mechanism for the treatment of depression that we've seen in probably over 20 years***.

(emphasis added).

180. The bolded statement referenced above, and specifically the statement that "*the folks who see the data really understand that 5461 has the opportunity to be a really revolutionary medication because its going to be one - really, it's the first new mechanism for the treatment of depression that we've seen in probably over 20 years*," omitted that the FDA had not, at any point, determined that the dataset for efficacy evaluation was acceptable, and in fact had conveyed to Alkermes numerous times that it did not endorse significant portions of Alkermes' analyses. As discussed *supra* in ¶¶ 41, 64-65, 101, 141, 157, and 171, Alkermes and Defendant Frates knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made.

AA. The November 2017 Jefferies Global Healthcare Conference

181. On November 15, 2017, Defendant Frates characterized ALKS 5461 during the Jefferies Global Healthcare Conference as "[a] potential blockbuster for adjunctive treatment of major depressive disorder," and further stated, "***[s]o we're looking to both acceptance of the file,*** an advisory board because it's a new mechanism in '18 ***and ultimately, approval***" (emphasis added). The bolded statements referenced in this paragraph omitted that at multiple times the FDA explicitly stated to Alkermes that it had significant, fundamental concerns with multiple elements of the clinical development program. As discussed *supra* in ¶¶ 41, 64-65, 101, 141, 157, and 171, Alkermes and Defendant Frates knew or recklessly disregarded that the above-bolded statements were false and misleading when the statements were made.

BB. The April 2, 2018 Alkermes Conference Call on ALKS 5461 Regulatory Update

182. On April 2, 2018 the Company announced that it had received an RTF from the FDA regarding ALKS 5461. In announcing the RTF, Defendant Pops stated:

> So Friday evening, we received a Refusal to File letter from the FDA for the new drug application for ALKS 5461 for the adjunctive treatment of major depressive disorder. To say that we were surprised is an understatement. The NDA we submitted in January included data from more than 30 clinical trials in more than 1,500 patients with MDD. We believe strongly that throughout the clinical development program, ALKS 5461 demonstrated a consistent profile of antidepressant activity, safety and tolerability. ***We have had many interactions with the FDA over many years culminating in a pre-NDA meeting last summer,*** which led to the commencement of a rolling submission. While we expected there to be questions during the review process, ***in none of these transactions did [the] FDA raise concerns, which would have led us to expect an RTF.***

183. The bolded statements referenced above, and specifically the statement that the Company "*had many interactions with the FDA over many years culminating in a pre-NDA meeting last summer . . . in none of these transactions did [the] FDA raise concerns, which would have led us to expect an RTF*" blatantly omitted that at multiple times the FDA explicitly stated to

Alkermes that it had significant, fundamental concerns with multiple elements of the clinical development program. As discussed *supra* in ¶¶ 41, 64-65, 101, 141, 157, and 171, Alkermes and Defendant Pops knew or recklessly disregarded that the above-bolded statements were false and misleading when the statements were made.

184. Analysts reacted negatively to the revelation of the problems behind the RTF and to the RTF itself. That same day, for example, Cantor Fitzgerald issued an analyst report noting that the FDA response stood "in stark contrast to a comment by the CEO on 2Q17 results conference call. . . . [***W]e believe investors may have been led to believe that FDA viewed the ALKS 5461 data potentially adequate for approval***. That the FDA has asked for additional clinical studies strongly calls into question such an assumption, in our opinion" (emphasis added). J.P. Morgan also issued an analyst report the same day noting the FDA's "relatively extreme" language regarding questions around effectiveness and need for additional data, and "completely removed the product from [J.P. Morgan's] model pending additional updates." In a separate update, J.P. Morgan stated that "[t]he RTF for 5461 is clearly not a good start. This letter also appears to be particularly bad with comments around overall effectiveness (unusual for an RTF) and the need for additional clinical trials."

CC. The April 16, 2018 Form 8-K, Press Release, and Conference Call

185. On April 16, 2018, Alkermes issued a press release announcing that the FDA had rescinded its initial RTF letter, issued March 30, 2018, and thus accepted for review the NDA for ALKS 5461. The press release was also filed with the SEC as an exhibit to a Form 8-K signed by David Gaffin, Senior Vice President and Chief Legal Officer and Secretary.

186. The same day, the Company held a conference call to discuss the FDA's acceptance of the NDA for ALKS 5461. During the conference call, Defendant Pops gave the following explanation regarding the initial FDA RTF:

> When we received the RTF, ***it was immediately apparent to us that the stated basis for the Refusal to File was inconsistent with the content of the NDA and our prior interactions with the agency***. We were hopeful that these differences could be resolved following conversations with them, and to FDA's credit, that is precisely what occurred.
>
> * * *
>
> The RTF was based on two observations. ***First was that the application contained insufficient evidence of overall effectiveness. The basis for that statement did not reflect a complete understanding of the NDA submission, and we directed FDA to the relevant information in the NDA***. The second was the lack of adequate bridging between 5461 and the RLD, buprenorphine. We raised this with the FDA, and they agreed that this was not the basis for an RTF. Both of these issues will be addressed within the context of the review.
>
> * * *
>
> The NDA includes data for more than 30 clinical trials and more than 1,500 patients with MDD. ***We believe strongly that throughout the clinical development program, ALKS 5461 has demonstrated a consistent profile of antidepressant activity, safety and tolerability in the adjunctive treatment of MDD. We have had many interactions with FDA over the years, leading to a pre-NDA meeting last summer, our rolling submission, the completeness of that submission in January, and the appropriate and timely resolution of the RTF and acceptance of the filing.***

187. The bolded statements referenced above, and in particular the statements that "*the stated basis for the Refusal to File was inconsistent with . . . our prior interactions with the agency*"; "*[t]he basis for th[e statement that the application contained insufficient evidence of overall effectiveness] did not reflect a complete understanding of the NDA submission*"; and "*[w]e believe strongly that throughout the clinical development program, ALKS 5461 has demonstrated a consistent profile of antidepressant activity, safety and tolerability in the adjunctive treatment of MDD*" omitted that the FDA had conveyed to Alkermes numerous times that it did not endorse significant portions of Alkermes' analyses, and that the FDA had significant, fundamental

concerns with multiple elements of the clinical development program surrounding efficacy. As discussed *supra* in ¶¶ 41, 64-65, 101, 141, 157, and 171, Alkermes and Defendant Pops knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made

DD. The April 26, 2018 Earnings Call

188. On April 26, 2018, Defendant Pops stated during an earnings call that:

> ***Our belief from the outset has been that a rigorous and comprehensive review of the complete dataset supporting the application, including safety, efficacy and benefit/risk profile, with*** [sic] ***support approval of 5461*** and provide an important new medication for patients.
>
> * * *
>
> ***Our confidence in the 5461 data package is unwavering and is based on the foundation of data generated from the clinical development program of more than 30 clinical trials and more than 1,500 patients with MDD.***

189. The bolded statements referenced above, and in particular the statements that "*[o]ur belief from the outset has been that a rigorous and comprehensive review of the complete dataset supporting the application, including safety, efficacy and benefit/risk profile, with* [sic] *support approval of 5461*" and "*[o]ur confidence in the 5461 data package is unwavering and is based on the foundation of data generated from the clinical development program of more than 30 clinical trials and more than 1,500 patients with MDD"* were false and misleading because they omitted that the FDA had conveyed to Alkermes numerous times that it did not endorse significant portions of Alkermes' analyses, and that the FDA had significant, fundamental concerns with multiple elements of the clinical development program surrounding efficacy. As discussed *supra* in ¶¶ 41, 64-65, 101, 141, 157, and 171, Alkermes and Defendant Pops knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and

misleading when the statements were made.

EE. The May 2018 Deutsche Bank Health Care Conference

190. During the May 9, 2018 Deutsche Bank Health Care Conference, Defendant Jackson stated:

> [W]e filed our NDA, ***our registration package is quite robust consisting of over 30 clinical studies and safety data in over 1,500 patients. Our clinical response has been consistent across all the studies that we've performed, and we have a very clean and robust safety profile***, allowing for a strong benefit/risk ratio for this product. So we anticipate a potential advisory committee meeting for this product by the fourth quarter of this year and we're preparing, as we speak, to pursue that. Additionally, in parallel with our development efforts, we're kicking off some of our precommercialization activities.

191. The bolded statements referenced above, and specifically the statements that "*our registration package is quite robust consisting of over 30 clinical studies and safety data in over 1,500 patients*" and "*[o]ur clinical response has been consistent across all the studies that we've performed, and we have a very clean and robust safety profile*" were false and misleading because they omitted that the FDA had conveyed to Alkermes numerous times that it did not endorse significant portions of Alkermes' analyses, and that the FDA had significant, fundamental concerns with multiple elements of the clinical development program surrounding efficacy. As discussed *supra* in ¶¶ 41, 64-65, 101, 141, 157, and 171, Alkermes and Defendant Jackson knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made.

FF. The May 2018 UBS Global Healthcare Conference

192. Similarly, during the May 21, 2018 UBS Global Healthcare Conference, Defendant Jackson stated:

> ***Now our registration package for ALKS 5461 is quite robust.*** As I mentioned earlier, we filed the program at the beginning of this year,

> and ***it consists of over 30 clinical studies and safety exposure in over 1,500 different patients. The efficacy that we've seen in this program has been consistent across all the studies that we've performed. And we've seen a really strong and clean safety profile, leading to a great benefit-risk ratio with this product.*** So this puts us in a position, as I mentioned earlier, to be ready for an Advisory Committee towards the end of the year, and we're actively working and preparing for that meeting as we speak

193. The bolded statements referenced above, and in particular the statements that "*our registration package for ALKS 5461 is quite robust*"; "*[t]he efficacy that we've seen in this program has been consistent across all the studies that we've performed*"; and "*we've seen a really strong and clean safety profile, leading to a great benefit-risk ratio with this product*" were false and misleading because they omitted that the FDA had conveyed to Alkermes numerous times that it did not endorse significant portions of Alkermes' analyses, and that the FDA had significant, fundamental concerns with multiple elements of the clinical development program surrounding efficacy. As discussed *supra* in ¶¶ 41, 64-65, 101, 141, 157, and 171, Alkermes and Defendant Jackson knew or recklessly disregarded that the statements referenced in the preceding paragraph were false and misleading when the statements were made.

GG. The June 2018 Goldman Sachs Global Healthcare Conference

194. During the June 13, 2018 Goldman Sachs Global Healthcare Conference, Defendant Pops stated:

> ***So in totality, we believe that the evidence supporting the licensure of 5461 is quite strong because even in the negative studies, you see signals of how the drug is paving and one can see quite explicitly that the difference between a negative study and a positive study in our data are the difference in the way the control group or the placebo group, which I had mentioned is actually getting SSRIs as well, is behaving. So the ability to attenuate placebo response in large outpatient studies over long periods of time is one of the tricks of the trade that one learns over time.*** So we competed the submission of that NDA in January, and we had the excursion with FDA at the end of March on the Refuse to File, which was really a procedural misstep, and that was rectified within

> 2 weeks. And so now the review is underway. And I expect the next input that you'll get or that the Street will get will be as we move into the mid-cycle, late-cycle review and as we prepare for an Advisory Committee in the fourth quarter.

195. In response to a question from a Goldman Sachs analyst asking what key topics Alkermes anticipated from the upcoming Advisory Committees, Defendant Pops stated:

> ***I think the question comes down to the study designs that we employ, which were new, they weren't radically new, they're just derivative of previous study designs that have been used in depression; and the analytical methods that we used to analyze the data, which we think are more precise estimates of the effect sizes than the more traditional ones.*** But because they're both new, they're new, and so there's not a historical precedence to say, "Aha, this is a square peg that goes into a square hole at FDA."

196. The bolded statements referenced above, and in particular the statements "*we believe that the evidence supporting the licensure of 5461 is quite strong*" and "*the study designs that we employ . . . they weren't radically new, they're just derivative of previous study designs that have been used in depression; and the analytical methods that we used to analyze the data, which we think are more precise estimates*" were false and misleading because they omitted that the FDA had conveyed to Alkermes numerous times that it did not endorse significant portions of Alkermes' analyses, and that the FDA had significant, fundamental concerns with multiple elements of the clinical development program surrounding efficacy. As discussed *supra* in ¶¶ 41, 64-65, 101, 141, 157, and 171, Alkermes and Defendant Pops knew or recklessly disregarded that the above-bolded statements were false and misleading when the statements were made.

HH. The July 2018 Earnings Call

197. On July 26, 2018, Alkermes held a conference call with securities analysts to discuss Alkermes' 2018 second quarter financial results. During the conference call, Defendant Pops stated:

> ***The strength of the 5461 program rests on the totality of the data.*** Important new data on the long-term safety, tolerability and durability of antidepressant-effective ALKS 5461 were recently represented at APA and ASCP. ***Data from our long-term open-label extension study demonstrated durable antidepressant effect with clinical improvement that progressed over a prolonged period of time and was then sustained. In the study, ALKS 5461 was generally well tolerated and demonstrated an AE profile consistent with that seen in the placebo-controlled study.*** You will continue to see additional publications throughout the course of the year, including manuscripts on the pivotal efficacy study, and the data we've collected that more fully characterize 5461 safety profile and low-risk-of-abuse potential.

198. The bolded statements referenced above, and in particular the statement that "*The strength of the 5461 program rests on the totality of the data. . . . Data from our long-term open-label extension study demonstrated durable antidepressant effect with clinical improvement that progressed over a prolonged period of time and was then sustained*," were false and misleading because they omitted that the FDA had conveyed to Alkermes numerous times that it did not endorse significant portions of Alkermes' analyses, and that the FDA had significant, fundamental concerns with multiple elements of the clinical development program surrounding efficacy. As discussed *supra* in ¶¶ 41, 64-65, 101, 141, 157, and 171, Alkermes and Defendant Pops knew or recklessly disregarded that the above-bolded statements were false and misleading when the statements were made.

II. The October 2018 Earnings Call

199. On October 23, 2018, Alkermes held a conference call with securities analysts to discuss Alkermes' 2018 third quarter financial results. During the conference call, Defendant Pops stated:

> As you know, 5461 is our novel opioid system modulator that we're developing for the adjunctive treatment of major depressive disorder. With a PDUFA date of January 31st, the regulatory review is well under way. The next milestone in the review process will take place next week November 1st with a joint meeting of the

> Psychopharmacologic Drugs and Drug Safety Advisory Committees at FDA.
>
> * * *
>
> ***You've heard me say time and again we believe that data generated in this large program support registration*** and that 5461 has the potential to provide benefit to patients through a new mechanism of action. At the same time, we're presenting FDA with an application that differs from what they're used to seeing, including new study designs and analysis. The AdCom will be an important determinant of the approvability of 5461 and we're ready to go.

200. The bolded statement referenced above, and in particular the statement that "*we believe that data generated in this large program support registration*," is false and misleading because it omitted that the FDA had conveyed to Alkermes numerous times that it did not endorse significant portions of Alkermes' analyses, and that the FDA had significant, fundamental concerns with multiple elements of the clinical development program surrounding efficacy. As discussed *supra* in ¶¶ 41, 64-65, 101, 141, 157, and 171, Alkermes and Defendant Pops knew or recklessly disregarded that the above-bolded statement was false and misleading when the statement was made.

VII. LOSS CAUSATION

201. During the Class Period, as detailed herein, Defendants' material misrepresentations and omissions caused the price of Alkermes common stock to be artificially inflated and/or maintained such artificial inflation in the price of Alkermes common stock prior to and during the Class Period, thereby operating as a fraud or deceit upon Lead Plaintiff and other putative class members who purchased or otherwise acquired Alkermes common stock during the Class Period. As a result, Lead Plaintiffs and members of the Class were damaged when the artificial inflation gradually dissipated as a series of corrective disclosures entered the market concerning multiple elements of ALKS 5461's clinical development program.

202. In reliance upon public information disclosed by and relating to Alkermes and ALKS 5461, as well as the integrity of the market price for Alkermes common stock, Lead Plaintiff and other putative Class members purchased or otherwise acquired Alkermes common stock during the Class Period at artificially inflated prices that incorporated and reflected Defendants' material misrepresentations and omissions alleged herein. Lead Plaintiff and other putative Class members suffered actual economic loss and were damaged by Defendants' misrepresentations and omissions when the truth concerning ALKS 5461 was revealed through the public disclosures of new information concerning the FDA's repeated concerns regarding ALKS 5461. These partial corrective disclosures and/or materializations of the foreseeable risks concealed by Defendants' fraud caused foreseeable declines in the price of Alkermes common stock by removing portions of the artificial inflation in the price of Alkermes common stock that resulted from Defendants' fraud. Moreover, the timing and magnitude of the declines in the price of Alkermes common stock in response to the public disclosure of new, Company-specific news on each of the foregoing days, as alleged herein, negate any inference that the losses suffered by Lead Plaintiff and other Class members were caused by changed market conditions or other macroeconomic factors unrelated to Defendants' fraud.

203. Specifically, on January 21, 2016, Alkermes announced that two of its three Phase 3 efficacy studies failed to meet their prespecified primary efficacy endpoints under FDA-approved protocols, but that the studies achieved statistical significance through *post hoc* analyses. Industry analysts interpreted the reference to "*post hoc* analyses"—the means by which Alkermes claimed to have reached "statistical significance" despite the failure to meet primary efficacy endpoints—to refer to Alkermes' use of SPCD, which Alkermes had disclosed at least by late 2013 as one of the methods to be used in its Phase 2 and 3 efficacy studies. However, the investing

public was yet unaware that the FDA had, on multiple occasions, and as early as late 2013, expressed significant concerns to the Company regarding (and had specifically not authorized) the use of SPCD in the ALKS 5461 trials, or that the FDA had told Alkermes that while SPCD analysis could be used for its prior publicized "successful" proof-of-concept studies, it was not acceptable for its Phase 3 efficacy studies. Analysts reacted negatively to the disclosure of the results of the Phase 3 efficacy studies; J.P. Morgan, in an analyst report titled "Depressing Outcome for '5461; Still See Meaningful LT Value in ALKS But Stepping to Sidelines For Now" noted that "FORWARD-4 showed a clear trend towards benefit but ended up being a near miss that, according to management, would have hit if using different statistical methods."

204. In response to this revelation, the Company's stock price dropped 44.24% from a closing price of $60.42 on January 20, 2016, to close at $33.69 on January 21, 2016, on volume of 12,467,289 shares—more than five times Alkermes' average volume during the month of January.

205. Notwithstanding the new information concerning the results of the ALKS 5461 Phase 3 efficacy studies revealed on January 21, 2016, the full truth regarding ALKS 5461's NDA prospects was not revealed at that time, as Defendants continued to hide the FDA's skepticism and concerns regarding Alkermes' use of SPCD in its studies from the general public for over two more years. As a result, Alkermes common stock continued to trade at artificially inflated prices.

206. The truth about ALKS 5461 was further partially revealed on April 2, 2018, when the FDA issued its initial RTF letter for ALKS 5461. This RTF letter publicly hinted at, for the first time, the FDA's skepticism and concerns surrounding the Company's testing methodologies and studies for ALKS 5461, which the FDA had extensively conveyed privately to Alkermes as early as ***five years*** prior and consistently thereafter. In issuing the RTF, the FDA "t[ook] the position that it is unable to complete a substantive review of the regulatory package, based on

insufficient evidence of overall effectiveness for the proposed indication, and that additional well-controlled clinical trials are needed prior to the resubmission of the NDA for ALKS 5461."

207. In response to this revelation, the Company's stock price dropped a stunning 22% from a closing price of $57.96 on March 29, 2018, to $45.23 on April 2, 2018, on volume of 8,053,845 shares, approximately ten times Alkermes' average volume during the prior month of March, and reflecting a loss in market capitalization of almost $2 billion.

208. Analysts reacted negatively to this revelation. For example, that same day, Cantor Fitzgerald issued an analyst report noting that the FDA response stood "in stark contrast to a comment by the CEO on 2Q17 results conference call. ***We believe investors may have been led to believe that FDA viewed the ALKS 5461 data potentially adequate for approval***" (emphasis added). J.P. Morgan also issued an analyst report noting the FDA's "relatively extreme" language regarding questions around effectiveness and need for additional data, and "completely removed the product from [J.P. Morgan's] model pending additional updates." In a separate update, J.P. Morgan noted that the letter "appears to be particularly bad with comments around overall effectiveness (unusual for an RTF) and the need for additional clinical trials." Morgan Stanley's analyst report similarly stated that "***RTF on 5461 NDA is a negative surprise*** following Alkermes' Feb 14 guidance call which included an assumption of sales rep hiring in 2H:18" (emphasis added).

209. On April 16, 2018, the Company announced that the FDA had reversed course and accepted for review the NDA for ALKS 5461. In response, the price of the Company's common stock recovered approximately 4.5%, from a closing price of $42.53 per share on April 13, 2018, to $44.43 on April 16, 2018, on volume of 6,109,238 shares—nearly 4.3 times Alkermes' average volume in the days since the initial RTF letter. The Company's announcement, however, continued to withhold material facts from the investing public, as detailed above.

210. In an April 26, 2018 Form 8-K, the Company continued to express confidence in ALKS 5461, stating that "[t]he regulatory review of ALKS 5461 is back on track and we continue to prepare for potential approval and launch in 2019." Subsequently, the Company's common stock price recovered approximately 4.5%, from a closing price of $44.07 per share on April 25, 2018, to $46.05 on April 26, 2018.

211. Notwithstanding the new information concerning ALKS 5461 revealed on April 2, 2018, the full truth regarding ALKS 5461's NDA prospects was not revealed at that time, as Defendants continued to make material misrepresentations and omit material facts regarding these matters from their public statements concerning the drug and relating application. As a result, Alkermes common stock continued to trade at artificially inflated prices.

212. On Tuesday, October 30, 2018 the FDA released its Briefing Document. *Dow Jones Institutional News* reported at 9:01 am that day that "Alkermes PLC (ALKS) shares dropped 6.5% in Tuesday premarket trade after briefing documents for an upcoming Food and Drug Administration advisory committee meeting raised major questions about the company's depression drug[.]" Over the course of the day, the price of Alkermes common stock dropped from a closing price of $40.37 on October 29, 2018, to $39.80 on October 30, 2018, marking a single-day decline of 1.4%.

213. The inevitable truth was revealed more fully when, on November 1, 2018, the FDA's Advisory Committees held their public meeting, discussed the drug, gave further detail on the regulatory history for ALKS 5461, including their concerns regarding the ALKS 5461 clinical development program, and then voted 21 to 2 against the approval of ALKS 5461. In response, the price of Alkermes common stock plummeted 7.57% from a closing price of $40.83 on October 31, 2018 (trading was halted on November 1, 2018), to $37.74 on November 2, 2018, reflecting a

loss of $480 million in market capitalization. Analysts expressed surprise at the information that they recognized had been withheld by Alkermes. For example, in a report that day, Credit Suisse wrote "Extent of Differences Between FDA and Company Surprising: . . . It was surprising to us today to hear the amount of disagreement the FDA has on fundamental issues related to the ALKS 5461 program such as how the studies should have been designed and how many of the trials were actually positive and supportive of approval. We are also somewhat surprised by the relative optimism the Alkermes team still maintained for ALKS 5461 despite what were clearly significant objections that must have been voiced by the FDA during the development and review process." An Evercore ISI analyst wrote on November 1, "The negative AdCom vote isn't a surprise per se. However, what did catch my attention was the FDA rebuke on how company didn't appear to heed to [*sic*] FDA advice on trial design and endpoints." Jefferies also wrote on the same day, "For many committee members, the last minute change ***and disregard for FDA's guidance was concerning***, especially given that MADRS-6 excludes many important categories important in evaluating depression such as lack of sleep, appetite, and suicidal ideation" (emphasis added).

214. In sum, as news was revealed to the market concerning the truth about the developmental program for ALKS 5461, the Company's stock price fell initially by 44% after a partial corrective disclosure in January 2016 and experienced drops in April, October, and November 2018 of 22%, 1.4%, and 7.57%, respectively, resulting in a total loss of $6.7 billion in market capitalization.

215. Each of these stock price declines was caused by the disclosure of previously concealed or unknown information relating to the material misstatements and omissions alleged herein.

216. Had Lead Plaintiff and the Class known of the material adverse information alleged

herein, they would not have purchased Alkermes common stock at artificially inflated prices and they would not have proximately suffered losses as the previously-withheld information was revealed to the market.

VIII. INAPPLICABILITY OF THE STATUTORY SAFE HARBOR

217. The statutory safe harbor applicable to forward-looking statements under certain circumstances does not apply to any of the false and misleading statements pled in this Complaint. None of the misstatements and omissions complained of herein was a forward-looking statement, nor were any of the statements identified as forward-looking when made. Rather, the false or misleading statements and omissions complained of in this Complaint concerned omissions of historical and/or current facts and conditions existing at the time the statements were made.

218. Alternatively, to the extent that any of the false or misleading statements alleged herein can be construed as forward-looking statements, they were not accompanied by any meaningful cautionary language identifying important facts that could cause actual results to differ materially from those in the purportedly forward-looking statements. Alternatively, to the extent the statutory safe harbor would otherwise apply to any forward-looking statements pleaded herein, Defendants are liable for those false or misleading forward-looking statements because at the time those statements were made, the speaker(s) knew the statement was false or misleading, or the statement was authorized and/or approved by an executive officer of Alkermes who knew that the statement was materially false or misleading when made.

IX. PRESUMPTION OF RELIANCE

219. Plaintiffs are entitled to a presumption of reliance under *Affiliated Ute Citizens of Utah v. U.S.*, 406 U.S. 128 (1972), because the claims asserted herein against Defendants are predicated in part upon material omissions of fact that Defendants had a duty to disclose.

220. In the alternative, Plaintiffs are entitled to a presumption of reliance on Defendants'

material misrepresentations and omissions pursuant to the fraud-on-the-market doctrine because, at all relevant times, the market for Alkermes common stock was open, efficient and well-developed for the following reasons, among others:

i. The market for Alkermes common stock was, at all relevant times, an efficient market that promptly digested current information with respect to the Company from all reliable, publicly-available sources and reflected such information in the price of Alkermes common stock;

ii. Alkermes common stock met the requirements for listing and was listed and actively traded on the NASDAQ, a highly efficient and automated market;

iii. The Company was consistently followed, before and throughout the Class Period, by the media. Alkermes was followed by numerous securities analysts employed by firms including Cantor Fitzgerald, Credit Suisse, J.P. Morgan, Barclays, and Morgan Stanley, among others, who wrote reports about the Company and the value of its common stock that were publicly available and entered the public marketplace;

iv. The price of Alkermes common stock reacted promptly to the dissemination of new information regarding the Company, as set forth above. Alkermes common stock was actively traded throughout the Class Period, with substantial trading volume and average weekly turnover and high institutional investor participation;

v. Alkermes regularly communicated with public investors through established market communication mechanisms, including through regular press releases, which were carried by national and international news wires, and through other wide-ranging public disclosures, such as communications and conferences with investors, the financial press, and other similar reporting services; and

vi. As a public company, Alkermes filed periodic public reports with the SEC.

221. As a result of the foregoing, the market for Alkermes common stock promptly digested current information regarding Alkermes from all reliable, publicly available sources and reflected such information in the price of Alkermes' common stock. Under these circumstances, purchasers of Alkermes common stock during the Class Period suffered injury through their purchase of Alkermes common stock at artificially inflated prices and a presumption of reliance applies.

222. Accordingly, Lead Plaintiff and other members of the Class did rely and are entitled to have relied upon the integrity of the market price for Alkermes common stock and to a presumption of reliance on Defendants' materially false and misleading statements and omissions during the Class Period. Additionally, Lead Plaintiff is entitled to a presumption of reliance because the claims asserted herein against Defendants are also predicated upon omissions of material fact which there was a duty to disclose.

X. CLASS ACTION ALLEGATIONS

223. Lead Plaintiff brings this action on behalf of themselves and as a class action pursuant to Federal Rule of Civil Procedure 23(a) and (b)(3) on behalf of a class consisting of all persons and entities who purchased or acquired Alkermes common stock during the period from July 31, 2014 through and including November 1, 2018 (the "Class"), and who were damaged thereby. Excluded from the Class are: (a) Defendants; (b) members of the immediate families of the Individual Defendants; (c) the subsidiaries and affiliates of Defendants; (d) any person or entity who is a partner, executive officer, director or controlling person of Alkermes (including any of its subsidiaries or affiliates) or any other Defendant; (e) any entity in which any Defendant has a controlling interest; (f) Defendants' directors' and officers' liability insurance carriers, and any affiliates or subsidiaries thereof; and (g) the legal representatives, heirs, successors and assigns of any such excluded party.

224. The members of the Class are so numerous that joinder of all members is impracticable. Throughout the Class Period, Alkermes common stock was actively traded on the NASDAQ. As of June 12, 2019, the Company had over 156 million shares of common stock issued and outstanding. The precise number of Class members is unknown to Lead Plaintiff at this time, but it is believed to be in the thousands.

225. A class action is superior to other available methods for the fair and efficient

adjudication of this controversy. Because the damages suffered by individual Class members may be relatively small, the expense and burden of individual litigation make it impracticable for Class members individually to seek redress for the wrongful conduct alleged herein.

226. Lead Plaintiff's claims are typical of the claims of the members of the Class as all members of the Class are similarly affected by Defendants' respective wrongful conduct in violation of the federal laws complained of herein.

227. Lead Plaintiff will fairly and adequately protect the interests of the members of the Class and have retained counsel competent and experienced in class and securities litigation. Lead Plaintiff has no interests antagonistic to or in conflict with those of the Class.

228. Common questions of law and fact exist as to all members of the Class and predominate over any questions solely affecting individual members of the Class. Among the questions of law and fact common to the Class are:

i. whether the federal securities laws were violated by Defendants' respective acts as alleged herein;

ii. whether the SEC filings, press releases, reports and other public statements disseminated to the investing public during the Class Period contained material misstatements or omitted to state material information;

iii. whether and to what the extent the market prices of the Company's common stock were artificially inflated during the Class Period due to the non-disclosures and/or misrepresentations complained of herein;

iv. whether Defendants acted with scienter;

v. whether, with respect to Lead Plaintiff's claims pursuant to Section 20(a) of the Exchange Act, the Individual Defendants named in those claims were controlling persons of the Company;

vi. whether reliance may be presumed pursuant to the fraud-on-the-market doctrine; and

vii. whether the members of the Class have sustained damages as a result of the misconduct complained of herein, and if so, the proper measure thereof.

229. The names and addresses of those persons and entities who purchased Alkermes' common stock during the Class Period are available from the Company's transfer agent(s). Notice may be provided to such purchasers and/or record owners via first class mail using techniques and a form of notice similar to those customarily used in securities class actions.

XI. CLAIMS FOR RELIEF

COUNT ONE

Violation of Section 10(b) of the Exchange Act and Rule 10b-5 Promulgated Thereunder Against All Defendants

230. Lead Plaintiff repeats and realleges each and every allegation contained above as if fully set forth herein.

231. During the Class Period, Defendants carried out a plan, scheme, and course of conduct which was intended to and, throughout the Class Period, did: (i) deceive the investing public regarding Alkermes' business, operations, management and the intrinsic value of Alkermes common stock; (ii) enable Defendants to artificially inflate the price of Alkermes common stock; and (iii) cause Lead Plaintiff and other members of the Class to purchase Alkermes common stock at artificially inflated prices. In furtherance of this unlawful scheme, plan, and course of conduct, Defendants jointly and individually (and each of them) took the actions set forth herein.

232. Defendants (i) employed devices, schemes, and artifices to defraud; (ii) made untrue statements of material fact and/or omitted to state material facts necessary to make the statements not misleading; and (iii) engaged in acts, practices, and a course of business which operated as a fraud and deceit upon the purchasers of the Company's common stock in an effort to maintain artificially high market prices for Alkermes' common stock in violation of Section 10(b) of the Exchange Act and Rule 10b-5. All Defendants are sued either as primary participants in the wrongful and illegal conduct charged herein or as controlling persons as alleged below.

233. Defendants, individually and in concert, directly and indirectly, by the use, means or instrumentalities of interstate commerce and/or of the mails, engaged and participated in a continuous course of conduct to conceal adverse material information about the business, operations and future prospects of Alkermes as specified herein.

234. These Defendants employed devices, schemes, and artifices to defraud, while in possession of material adverse non-public information and engaged in acts, practices, and a course of conduct as alleged herein in an effort to assure investors of Alkermes' value and performance and continued substantial growth, which included the making of, or the participation in the making of, untrue statements of material facts, and omitting to state material facts necessary in order to make the statements made about Alkermes and its business operations and future prospects in light of the circumstances under which they were made not misleading, as set forth more particularly herein, and engaged in transactions, practices, and a course of business which operated as a fraud and deceit upon the purchasers of Alkermes common stock during the Class Period.

235. Defendant Alkermes is liable for all materially false and misleading statements made during the Class Period, as alleged above.

236. Alkermes is further liable for the false and misleading statements made by Alkermes officers in press releases, during conference calls, and at conferences with investors and analysts, as alleged above, as the maker of such statements.

237. The Individual Defendants, as top executive officers of the Company, are liable as direct participants in the wrongs complained of herein. Through their positions of control and authority as officers of the Company, each of the Individual Defendants was able to and did control the content of the public statements disseminated by Alkermes. The Individual Defendants had direct involvement in the daily business of the Company and participated in the preparation and

dissemination of Alkermes' false and misleading statements as set forth above.

238. In addition, the Individual Defendants are liable for all materially false and misleading statements made during the Class Period, as alleged above.

239. The allegations above establish a strong inference that Defendants acted with scienter throughout the Class Period in that they had actual knowledge of the misrepresentations and omissions of material facts set forth herein, or acted with reckless disregard for the truth in that they failed to ascertain and to disclose such facts. Such Defendants' material misrepresentations and/or omissions were done knowingly or with recklessness for the purpose and effect of concealing Alkermes' operating condition and future business prospects from the investing public and supporting the artificially inflated price of its securities. As demonstrated by Defendants' material misstatements and omissions throughout the Class Period, if they did not have actual knowledge of the misrepresentations and omissions alleged, Defendants were reckless in failing to obtain such knowledge by recklessly refraining from taking those steps necessary to discover whether those statements were false or misleading.

240. As a result of the dissemination of the materially false and misleading information and failure to disclose material facts, as set forth above, the market price of Alkermes securities was artificially inflated during the Class Period. In ignorance of the fact that market prices of Alkermes' publicly-traded common stock were artificially inflated, and relying directly or indirectly on the false and misleading statements made by Defendants, or upon the integrity of the market in which the securities trade, and/or on the absence of material adverse information that was known to or recklessly disregarded by Defendants but not disclosed in public statements by them during the Class Period, Lead Plaintiff and the other members of the Class acquired Alkermes common stock during the Class Period at artificially high prices and were damaged thereby.

241. At the time of said misrepresentations and omissions, Lead Plaintiff and other members of the Class were ignorant of their falsity, and Defendants' material omissions. Had Lead Plaintiff and the other members of the Class and the marketplace known the truth, they would not have purchased or otherwise acquired their Alkermes common stock, or, if they had acquired such common stock during the Class Period, they would not have done so at the artificially inflated prices which they paid.

242. By virtue of the foregoing, Defendants have violated Section 10(b) of the Exchange Act and Rule 10b-5 promulgated thereunder.

243. As a direct and proximate result of their wrongful conduct, Lead Plaintiff and the other members of the Class suffered damages in connection with their respective purchases and sales of the Company's common stock during the Class Period.

COUNT TWO

Violation of Section 20(a) of the Exchange Act Against the Individual Defendants

244. Lead Plaintiff repeats and realleges each and every allegation contained above as if fully set forth herein.

245. The Individual Defendants acted as controlling persons of Alkermes within the meaning of Section 20(a) of the Exchange Act as alleged herein. By virtue of their high-level positions, and their ownership and contractual rights, participation in and/or awareness of the Company's operations and/or intimate knowledge of the false financial statements filed by the Company with the SEC and disseminated to the investing public, the Individual Defendants had the power to influence and control and did influence and control, directly or indirectly, the decision-making of the Company, including the content and dissemination of the various statements which Lead Plaintiff contends are false and misleading. The Individual Defendants

were provided with or had unlimited access to copies of the Company's reports, press releases, public filings and other statements alleged by Lead Plaintiff to be misleading prior to and/or shortly after these statements were issued and had the ability to prevent the issuance of the statements or cause the statements to be corrected.

246. In particular, each of the Individual Defendants had direct and supervisory involvement in the day-to-day operations of the Company and, therefore, is presumed to have had the power to control or influence the particular transactions giving rise to the securities violations as alleged herein, and exercised the same.

247. As set forth above, the Individual Defendants each violated Section 10(b) and Rule 10b-5 by their acts and omissions as alleged in this Complaint. By virtue of their positions as controlling persons, the Individual Defendants are liable pursuant to Section 20(a) of the Exchange Act. As a direct and proximate result of Defendants' wrongful conduct, Lead Plaintiff and other members of the Class suffered damages in connection with their purchases of the Company's common stock during the Class Period.

XII. PRAYER FOR RELIEF

WHEREFORE, Lead Plaintiff prays for relief and judgment, including:

A. determining that this action is a proper class action and certifying Lead Plaintiff as class representative under Rule 23 of the Federal Rules of Civil Procedure;

B. awarding compensatory damages in favor of Lead Plaintiff and the other Class members against all Defendants, jointly and severally, for all damages sustained as a result of the Defendants' wrongdoing, in an amount to be proven at trial, including interest thereon;

C. awarding Lead Plaintiff and the Class their reasonable costs and expenses incurred in this action, including counsel fees and expert fees; and

D. awarding Lead Plaintiff and the Class such other relief as may be deemed

appropriate by the Court.

JURY TRIAL DEMANDED

Lead Plaintiff hereby demands a trial by jury.

Date: July 9, 2019

Respectfully submitted,

/ s / Carol V. Gilden

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Attorneys for the Midwest Operating Engineers Pension Trust Fund and Lead Counsel for the Class

CERTIFICATION

Thomas M. Bernstein, Administrative Manager of the Midwest Operating Engineers Pension Trust Fund ("Midwest Operating Engineers"), declares, as to the claims asserted under the federal securities laws, that:

1. I am authorized to make this certification on behalf of Midwest Operating Engineers.

2. I have reviewed a complaint filed in this matter and wish to serve as a lead plaintiff.

3. Midwest Operating Engineers did not purchase the securities that are the subject of this action at the direction of its counsel or to participate in this action.

4. Midwest Operating Engineers is willing to serve as a lead plaintiff and class representative on behalf of the Class, including providing testimony at deposition and trial if necessary.

5. Midwest Operating Engineers' transactions in the securities of Alkermes Public Limited Company that are the subject of this action are set forth in Schedule A, attached hereto.

6. During the three years prior to the date of this Certification, Midwest Operating Engineers has not sought to serve as a representative party for a class under the federal securities laws, except in this case.

7. Midwest Operating Engineers will not accept any payment for serving as a class representative on behalf of the class beyond its *pro rata* share of any recovery, except such reasonable costs and expenses (including lost wages) relating to the representation of the class as ordered or approved by the court.

I declare under penalty of perjury that the foregoing is true and correct. Executed this 9th day of July 2019.

Thomas M. Bernstein
Administrative Manager
Midwest Operating Engineers Pension Trust Fund

SCHEDULE A

Trade Date	Transaction Type	Shares	Share Price ($)
8/7/2014	Purchase	20,000	41.9599
11/6/2014	Sale	(300)	51.5689
11/6/2014	Sale	(14,700)	51.0501
11/18/2014	Sale	(15,000)	53.0989
11/24/2014	Sale	(5,000)	56.3066
12/22/2014	Sale	(2,900)	59.0744
12/31/2014	Sale	(1,800)	59.0021
1/2/2015	Sale	(2,600)	59.0499
1/5/2015	Sale	(2,700)	59.0555
1/13/2015	Sale	(10,000)	69.0636
3/17/2015	Purchase	10,000	65.9187
3/27/2015	Purchase	10,000	62.7648
4/2/2015	Purchase	15,000	60.148
4/28/2015	Purchase	10,000	58.0509
7/15/2015	Sale	(15,000)	69.015
9/14/2015	Sale	(10,000)	70.4029
9/21/2015	Sale	(100)	71.8697
9/21/2015	Sale	(2,000)	71.4
11/3/2015	Sale	(5,000)	73.0499
11/4/2015	Sale	(6,900)	72.0984
11/6/2015	Sale	(5,600)	72.0779
11/9/2015	Sale	(5,400)	72.1097
11/18/2015	Sale	(5,000)	73.6787

Trade Date	Transaction Type	Shares	Share Price ($)
1/22/2016	Purchase	800	33
1/22/2016	Purchase	22,000	34.8853
1/25/2016	Purchase	7,200	36.9301
1/26/2016	Purchase	10,000	34.977
2/10/2016	Purchase	9,200	31.7736
2/10/2016	Purchase	10,800	32.1059
3/8/2016	Purchase	35,000	33.0394
3/9/2016	Purchase	20,000	31.6783
4/21/2016	Sale	(25,000)	42.308
5/9/2016	Purchase	14,000	39.5054
11/16/2016	Sale	(200)	59.0331
11/17/2016	Sale	(11,600)	59.4728
11/17/2016	Sale	(16,800)	59.2539
11/18/2016	Sale	(1,100)	59.2128
11/21/2016	Sale	(300)	59.0102
11/21/2016	Sale	(9,000)	59.0482
1/5/2017	Sale	(14,900)	59.2912
1/5/2017	Sale	(100)	60.12
2/23/2017	Purchase	9,204	52.2387
2/23/2017	Purchase	11,000	52.845
2/24/2017	Purchase	4,796	52.3497
5/9/2017	Purchase	18,100	57.0918
5/9/2017	Purchase	1,900	57.0761
7/28/2017	Purchase	10,000	54.9702

Trade Date	Transaction Type	Shares	Share Price ($)
9/6/2017	Purchase	10,000	50.041
11/21/2017	Purchase	30,000	49.0201
4/6/2018	Purchase	35,000	42.1545
4/25/2018	Purchase	15,000	44.262